

# **ENFLURANE AND HALOTHANE ANAESTHESIA IN CHILDREN**

**Cardiac arrhythmias and  
stress response during  
adenoidectomy**

**Gisli H Sigurdsson**



**Lund 1983**



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To Birna, Hjalti, Þorbjörg and Halldór



## SAMMANFATTNING

Hjärtarytmier är vanliga vid operativa ingrepp i munhåla och svalg och allvarliga komplikationer förekommer, även hos i övrigt friska patienter. Denna undersökning behandlar differentialdiagnos, frekvens, orsaker samt förebyggande av ventrikulära arytmier vid inhalationsanestesi med enfluran och halotan hos barn under adenoidektomi.

EKG (inklusive esofagus-EKG), hjärtfrekvens, kapillära pulsationer, medelartärtryck, andningsfrekvens, thoraximpedans, end-tidal  $\text{CO}_2$  tension, blodgaser, plasmakoncentrationer av katekolaminer, ACTH, kortisol och  $17\text{-}\alpha\text{-hydroxyprogesteron}$  följdes under ingreppen.

Man fann att QRS-komplex av abnormalt utseende, som mest förekom under halotananestesi, vanligtvis var tecken på ventrikulär arytmi, och inte aberrant överledda slag av supraventrikulärt ursprung.

Förekomsten av ventrikulära arytmier var högst bland de barn som sövdes med halotan utan intubation. Intubation och kontrollerad andning reducerade arytmifrekvensen markant. När en effektiv premedicinering med diazepam, morfin och skopolamin användes, kunde förekomsten av ventrikulära arytmier närmast elimineras vid halotananestesi. Vid inhalationsinduktion med halotan för adenoidektomi rekommenderas därför en effektiv premedicinering, intubationsanestesi samt kontrollerad ventilation.

Vid enflurananestesi var arytmifrekvensen relativt låg, oavsett vilken anestesiteknik som användes. Däremot noterades mera uttalad andningsdepression vid enfluran jämfört med vid halotananestesi. Därför är intubation och kontrollerad andning också att föredraga vid enflurananestesi för dessa ingrepp.

This thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

- I Sigurdsson GH, Carlsson C, Lindahl S and Werner O.  
Cardiac arrhythmias in non-intubated children during adenoidectomy. A comparison between enflurane and halothane anaesthesia.  
*Acta Anaesthesiologica Scandinavica* 27:75, 1983.
- II Sigurdsson GH and Lindahl S.  
Cardiac arrhythmias in intubated children during adenoidectomy. A comparison between enflurane and halothane anaesthesia.  
*Acta Anaesthesiologica Scandinavica*, in press 1983.
- III Sigurdsson GH, Werner O and Fåhræus T.  
Ventricular arrhythmia or supraventricular arrhythmia with aberrant conduction? An electrocardiographic study in halothane-anaesthetized children undergoing adenoidectomy.  
*British Journal of Anaesthesia*, in press 1983.
- IV Sigurdsson GH, Lindahl S and Nordén N.  
Influence of premedication on plasma ACTH and cortisol concentrations in children during adenoidectomy.  
*British Journal of Anaesthesia* 54:1075, 1982.
- V Sigurdsson GH, Lindahl S and Nordén N.  
Catecholamine and endocrine response in children during enflurane and halothane anaesthesia for adenoidectomy.  
Submitted for publication 1983.
- VI Sigurdsson GH, Lindahl S and Nordén N.  
Influence of premedication on sympathetic-endocrine response and cardiac arrhythmias during halothane anaesthesia in children undergoing adenoidectomy.  
*British Journal of Anaesthesia*, in press 1983.

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## INTRODUCTION

The interest in cardiac arrhythmias during anaesthesia has existed since the beginning of this century, when Levy recorded arrhythmias during chloroform anaesthesia (1-4). Cannard and Dripps (5) demonstrated, in 1960, the clinical value of a continuous monitoring of ECG during anaesthesia. A more recent publication of Katz and Bigger (6) has shown that the occurrence of intraoperative cardiac arrhythmias varies widely (16 to 62%), depending on the patients age, pre-existing arrhythmias or heart disease, the method of anaesthesia and the operating site.

Many of the changes in cardiac rate and rhythm occurring during anaesthesia may be explained on the basis of altered autonomic balance, a preponderance of vagal or sympathetic activity producing characteristic changes (7,8,9). In addition, physiological and biochemical disturbances, such as baroreceptor reflexes, hypoxia, hypercarbia, changes in acid-base or electrolyte balance influence the diastolic depolarization of the subsidiary pacemakers of the heart (10,11,12).

Abnormalities of cardiac rhythm are not uncommon in children, but they differ in many respects from those observed in adults. The principal differences are related to etiology, the less stable autonomic system of childhood, and the greater facility of conduction through the A-V node at high rates (13). For example shifting of pacemaker from the S-A to the A-V node occurs commonly in children during increased parasympathetic activity. Adults more often have pre-existing heart disease as a cause of arrhythmias.

During the last decade, the occurrence of cardiac arrhythmias during oral surgery has been the subject of many investigations (14-17). The etiology of these has been related to a variety of factors, such as light anaesthesia, different anaesthetic agents and anaesthetic techniques, airway obstruction with resulting hypoxia and hypercarbia as well as surgery in sensitive reflex areas (6, 18-22). But the clinical significance of these arrhythmias has been debated (15,16,23). The majority of these, such

as A-V nodal rhythm, atrial ectopic rhythm or occasional unifocal ventricular ectopic beats are probably of benign nature and do not require treatment. However, frequent multifocal ventricular ectopic beats and ventricular tachycardia may indicate a serious physiological or pharmacological derangement of the cardiac function, which ultimately can result in ventricular fibrillation (6). This potential danger is substantiated in the literature. In an analysis of 48 deaths occurring during dental anaesthesia, Tomlin (24) suggested that one-third were associated with circulatory disturbances. Bourne (25) reported details of 16 deaths occurring during oral surgery in apparently healthy patients. Four of these had ventricular fibrillation and in 12 of the 16 patients no specific cause of death was found post mortem. Furthermore, Weigand (26) reported seven cases of cardiac arrest among almost 3000 patients undergoing adenoidectomy or tonsillectomy.

We have frequently observed disturbances in cardiac rhythm, ranging from sinus arrhythmia to chaotic ventricular rhythm, in children undergoing adenoidectomy. Since adenoidectomy is considered a minor surgical procedure and usually performed on otherwise healthy children, serious complications are not acceptable. The present study was designed to learn more about the mechanism of cardiac arrhythmias occurring during inhalational anaesthesia in children undergoing adenoidectomy.

#### PURPOSE OF THE STUDY

This series of investigations was focused on cardiac arrhythmias in anaesthetized children subjected to adenoidectomy. The aims were to study:

- \* incidence of arrhythmias with enflurane and halothane anaesthesia
- \* influence of anaesthetic technique
- \* differential diagnosis of arrhythmias
- \* effects of premedication on plasma ACTH and cortisol
- \* effects of enflurane and halothane on plasma catecholamines and ventricular arrhythmias
- \* premedication, plasma catecholamines and ventricular arrhythmias

## MATERIALS AND METHODS

### Patients

Threehundred and eightyfour children, between 1 and 12 years of age, were investigated, 299 undergoing adenoidectomy and 85 undergoing myringotomy (Table 1). No child had evidence of acute infection or of cardiopulmonary disease. The children, all out-patients, were fasted over night and were investigated between 8.30 and 10.30 a.m.

### Premedication

Two premedications were used. One consisted of 5 mg diazepam (Stesolid<sup>R</sup>; approximately  $0.25 \text{ mg kg}^{-1}$ ) rectally and 0.3-0.4 mg atropine (approximately  $0.015 \text{ mg kg}^{-1}$ ) sublingually (DA). The other was a rectal solution with diazepam (Apozepam<sup>R</sup>)  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$  (DMH). The premedication was ordered to be given 20-40 min before the induction of anaesthesia. A modification of the method described by Barker and Nisbet (27) (paper IV and VI) was used to evaluate sedative effects of the premedication. The assessment was done by an anaesthetist, who was not informed about which premedication was used.

### Monitoring devices

Subsequently, while the child was still awake and in the presence of one of the parents, ECG and thoracic impedance (paper I and II) electrodes were applied. A photoelectric transducer (Siemens-Elema, Stockholm) (28), for the assessment of capillary pulsation (paper I, II and IV), was attached to the distal part of the flexor side of the thumb and an arterial pressure cuff was placed around the arm. A calibrated infra-red carbon dioxide analyzer (130, Siemens-Elema, Stockholm) (29) was incorporated in the anaesthetic circuit. After induction of anaesthesia an unipolar oesophageal electrode was inserted with the help of a laryngoscope in 20 children (paper III). The tip of the electrode was placed so that the P wave was maximal.

Table 1  
Materials

| Investigation no.                       | I  |    |    |    | II |    |    | III | IV | V   |    |    |    | VI |    |     |
|-----------------------------------------|----|----|----|----|----|----|----|-----|----|-----|----|----|----|----|----|-----|
| Groups                                  | HM | EM | HA | EA | HS | ES | HC | Hoe | A  | B   | HN | EN | HI | EI | A  | B   |
| No. of patients                         | 46 | 39 | 46 | 36 | 25 | 25 | 25 | 20  | 7  | 7   | 7  | 7  | 7  | 7  | 40 | 40  |
| Premedication, DA */DMH**               | DA | DA | DA | DA | DA | DA | DA | DA  | DA | DMH | DA | DA | DA | DA | DA | DMH |
| Halothane/Enflurane, H/E                | H  | E  | H  | E  | H  | E  | H  | H   | H  | H   | H  | E  | H  | E  | H  | H   |
| Non-intubated/Intubated, N/I            | N  | N  | N  | N  | I  | I  | I  | N   | I  | I   | N  | N  | I  | I  | I  | I   |
| Spontaneous/Controlled ventilation, S/C | S  | S  | S  | S  | S  | S  | C  | S   | S  | S   | S  | S  | S  | S  | S  | S   |
| Adenoidectomy /Myringotomy, A/M         | M  | M  | A  | A  | A  | A  | A  | A   | A  | A   | A  | A  | A  | A  | A  | A   |

\* DA= diazepam approximately 0.25 mg kg<sup>-1</sup> and atropine approximately 0.015 mg kg<sup>-1</sup>  
 \*\*DMH= diazepam 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>



## Anaesthesia

Anaesthesia was induced via face-mask with  $O_2/N_2O$  ( $FiO_2$  0.25) administered for approximately one minute before halothane or enflurane was added and the  $O_2/N_2O$  ratio was adjusted to 1:1 ( $FiO_2$  0.5). The concentrations of halothane and enflurane were increased at intervals of 4-6 breaths, by steps of 0.5% and 1% respectively to a maximum of 2.5% for halothane and 5% for enflurane. In the children who underwent myringotomy, anaesthesia was maintained at 1-1.5% halothane or 2-3% enflurane (paper I). When the children, who underwent adenoidectomy, without endotracheal intubation, were clinically judged to be adequately anaesthetized, a mouth gag was inserted and the adenoidectomy was performed without further supply of anaesthetics. The children who were intubated, were manually ventilated for 15-20 sec before orotracheal intubation, which was performed without the use of muscle relaxants. These children received continuous supply of anaesthetics throughout the procedure. The children of all groups, except one (group HC of paper II), were allowed to breathe spontaneously during the procedure. A Mapleson D circuit with fresh gas flow of 3 times estimated minute ventilation was used to minimize rebreathing.

## Biochemical analysis

After the induction of anaesthesia a vein on the extensor surface of the hand was cannulated to allow blood sampling. Samples for analysis of venous oxygen ( $P_{VO_2}$ ) and carbon dioxide ( $P_{VCO_2}$ ) tensions were taken in syringes and kept on ice until the analysis were performed 10 min later (IL 413, Instrumentation Laboratories, Italy). ACTH was determined by radioimmunoassay (ACTHK, Sorin Biomedica, Italy), cortisol by solid phase radioimmunoassay (Gammacoat, Clinical Assays, Mass., USA) and a radioimmunochemical method was used for the assay of 17- $\alpha$ -hydroxyprogesterone (17 OHP) (OHPK, Sorin Biomedica, Italy). A modification of the radioenzymatic method of Passon and Peuler (30) (Upjohn Diagnostics, USA) was used for measuring total plasma catecholamine concentrations (paper V and VI).

### ECG criteria

Sinus tachycardia was not classified as an arrhythmia. Heart rate (HR) below  $60 \text{ min}^{-1}$  during 5 sec or more was defined as a sinus bradycardia (SB). Isolated ectopic beats were only reported when at least three were seen in the same child. In paper III the terms: "bizarre QRS configuration", "anomalous QRS complexes" and "anomalous beats" (13) were used to describe beats where the QRS complex was widened and its shape distinct from that of normally conducted sinus beats. Otherwise, beats with "bizarre QRS configuration" were considered to be ventricular (VES), unless there was positive evidence for a supraventricular origin. Three or more consecutive ventricular beats were regarded as ventricular tachycardia (VT).

### Measurements

ECG, capillary pulsation (CP), thoracic impedance (TI) and end-tidal carbon dioxide tension ( $P_{\text{ETCO}_2}$ ) were recorded continuously (Siemens-Elema, EM81). Heart rate (HR) and respiratory rate (f) were calculated from ECG recordings and end-tidal carbon dioxide curves, respectively. Systolic and diastolic arterial pressures were measured intermittently by auscultation and mean arterial pressure (MAP) was calculated. Measurements were made at the following stages:

- (1) before induction of anaesthesia
- (2) after induction of anaesthesia (approximately 2.5 min after start of induction)
- (3) during undisturbed anaesthesia (3.5-4.5 min after start of induction)
- (4) before intubation/before adenoidectomy (in the non-intubated children)
- (5) after intubation (only in intubated children)
- (6) during adenoidectomy
- (7) after adenoidectomy
- (8) at the end of anaesthesia, when the child was breathing normally and was judged to control its airways adequately, swallowing and reacting in a lively way to painful stimuli, but still not awake, "partial recovery"
- (9) 15 min postoperatively, when the child was awake.

Measurements of  $P_{ET}CO_2$  were not possible at stage 6 in the non-intubated children. Blood samples were taken at stages 3, 7 and 9.

### Statistics

Between-group comparisons were carried out with two-sided Student's t-test and the Chi-square test. In paper VI a step-wise linear discriminant analysis (31) was used to find all variables that contributed significantly to the discrimination between the groups. Probability values below 0.05 were considered to indicate statistical significance. The data in the text, tables and figures are given as mean values  $\pm$  standard error of the mean (SEM).

## RESULTS AND COMMENTS

### Paper I

This study was designed to investigate cardiac arrhythmias in non-intubated children undergoing adenoidectomy. The influence of two inhalational anaesthetics, enflurane and halothane, was evaluated. Children undergoing myringotomy constituted the control group (i.e. a non-oral surgery group).

With both anaesthetics cardiac arrhythmias occurred more often during adenoidectomy than during myringotomy. During both surgical procedures the total incidence of arrhythmias was higher with halothane than with enflurane anaesthesia (Table 2). A-V nodal rhythm was the most common arrhythmia in all groups. During adenoidectomy ventricular arrhythmias occurred in 41% of the children anaesthetized with halothane as compared to 3% with enflurane anaesthesia ( $p < 0.05$ ). Most of these arrhythmias appeared during surgery (Fig. 1). Unifocal VES were seen in six children, five developed multifocal VES and eight had ventricular tachycardia (Table 2). Two children developed a chaotic ventricular rhythm at a rate of about  $220 \text{ min}^{-1}$ . Circulatory symptoms, such as weak peripheral pulses and general pallor were noted, as illustrated by a decreased capillary pulsation (Fig. 2).

Table 2

Cardiac arrhythmias in non-intubated children during halothane and enflurane anaesthesia (1). All patients were premedicated with diazepam and atropine(DA) and were breathing spontaneously during the procedure.

| Anaesthetic agents             | MYRINGOTOMY |           | ADENOIDECTOMY |           |
|--------------------------------|-------------|-----------|---------------|-----------|
|                                | Halothane   | Enflurane | Halothane     | Enflurane |
| Groups                         | HM          | EM        | HA            | EA        |
| No. of children                | 46          | 39        | 46            | 36        |
| Arrhythmias total %            | 33          | 10        | 87***         | 39        |
| Supraventricular arrhythmias % | 22          | 10        | 74***         | 36        |
| Ventricular arrhythmias %      | 11          | 0         | 41*           | 3         |
| unifocal VES %                 | 2           | 0         | 13            | 0         |
| multifocal VES %               | 7           | 0         | 11            | 0         |
| ventricular tachycardia %      | 2           | 0         | 17            | 3         |

VES= ventricular ectopic beats. \*=  $p < 0.05$  and \*\*\*=  $p < 0.001$  for the difference between group HA and EA.

Anaesthesia without endotracheal intubation for adenoidectomy carries the risk of airway obstruction, with concomitant hypoxia and hypercarbia, two factors which are known to increase the incidence of ventricular arrhythmias during anaesthesia (20,21). In this study, however, airway obstruction was not common and only once observed in immediate relation to the occurrence of ventricular arrhythmia. Furthermore, venous as well as end-tidal  $\text{CO}_2$  tensions were higher and venous oxygen tensions lower with enflurane than with halothane anaesthesia. Thus, the difference in incidence of ventricular arrhythmias between the two agents, did not appear to be due to airway obstruction or difference in gas exchange.

The anaesthetic technique (without intubation) did not allow continued supply of anaesthetics during surgery, resulting in a more superficial anaesthesia towards the end of the procedure.





difference in occurrence of ventricular arrhythmias, since enflurane sensitizes the myocardium less in presence of catecholamines than halothane (33,34,35). However, the present study showed that the heart rate increased significantly more in the halothane group than in the enflurane group during surgery, especially in the children who developed ventricular arrhythmia. This indicated that there might have been a difference between the agents in catecholamine response during surgery. Thus, the low incidence of ventricular arrhythmias during enflurane anaesthesia may be explained by the combination of a reduced sympathetic response to surgery and decreased sensitivity of the myocardium to endogenous catecholamines (36). The usefulness of this agent was, however, limited in non-intubated children by early return of swallowing reflexes during surgery, which sometimes interfered with the procedure.

## Paper II

The objective of this investigation was to study the influence of endotracheal intubation on the occurrence of ventricular arrhythmias during enflurane and halothane anaesthesia in children undergoing adenoidectomy. The effects of controlled ventilation were also studied during halothane anaesthesia.

As in non-intubated children (paper I) cardiac arrhythmias were less frequent with enflurane than with halothane anaesthesia ( $p < 0.05$ ; Table 3) and A-V nodal rhythm was the most common arrhythmia with both anaesthetic agents also in this study. There was no statistically significant difference between the groups in incidence of ventricular arrhythmias, however, the more serious ones, such as multifocal ventricular ectopic beats and ventricular tachycardia were only seen among those who received halothane and were breathing spontaneously (group HS; Table 3). The children who received enflurane (group ES) and those who received halothane with controlled ventilation (group HC) only had occasional unifocal ventricular ectopic beats (Table 3). These arrhythmias generally lasted shorter time and had a slower rate compared with those seen in group HS. No adverse circulatory signs or symptoms were seen during these

arrhythmias as sometimes were noted in group HS.

Table 3

Cardiac arrhythmias in intubated children during halothane and enflurane anaesthesia (II). All patients were premedicated with diazepam and atropine (DA). Multifocal ventricular ectopic beats and ventricular tachycardia only occurred in group HS.

|                                   | SPONTANEOUS<br>VENTILATION |           | CONTROLLED<br>VENTILATION |
|-----------------------------------|----------------------------|-----------|---------------------------|
| Anaesthetic agent                 | Halothane                  | Enflurane | Halothane                 |
| Groups                            | HS                         | ES        | HC                        |
| No. of children                   | 25                         | 25        | 25                        |
| Arrhythmias total %               | 72*                        | 32        | 68                        |
| Supraventricular<br>arrhythmias % | 60*                        | 24        | 56                        |
| Ventricular<br>arrhythmias %      | 20                         | 8         | 12                        |
| unifocal VES %                    | 5                          | 8         | 12                        |
| multifocal VES %                  | 5                          | 0         | 0                         |
| ventricular tachycardia %         | 10                         | 0         | 0                         |

VES= ventricular ectopic beats. \*=  $p < 0.05$  for the difference between group HS and ES.

The end-tidal  $\text{CO}_2$  tension was significantly increased during anaesthesia and surgery in group HS and ES. The highest mean value ( $\pm$  SEM) in group HS was  $6.5 \pm 0.2$  kPa (Fig. 3; stage 5) and the highest single value noted was 7.7 kPa. In group ES the highest mean value was  $7.9 \pm 0.2$  kPa ( $p < 0.01$ ), with single values of 9.3 kPa found in two children of this group. In group HC the mean values for  $P_{\text{ET}}\text{CO}_2$  were kept between 5.2 and 5.4 kPa.

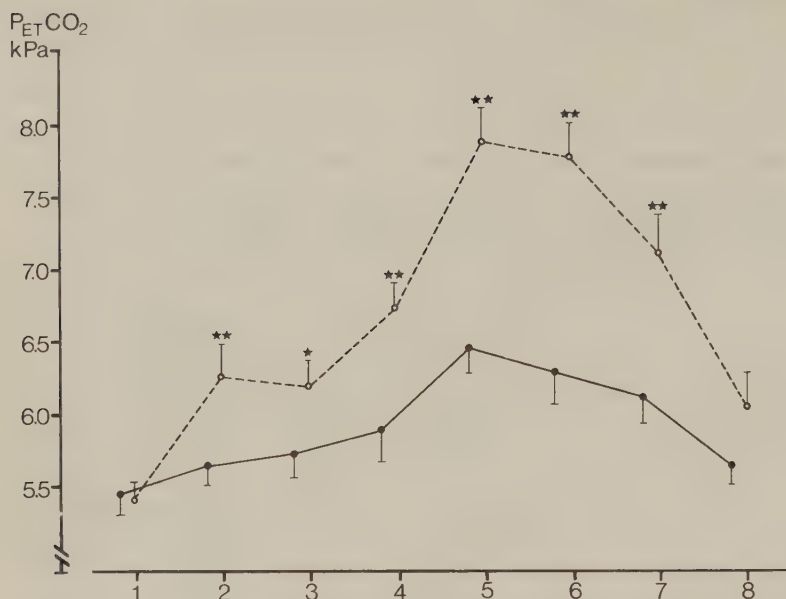


Fig. 3

End-tidal CO<sub>2</sub> tension (P<sub>ET</sub>CO<sub>2</sub>) (II) at different stages of the procedure (mean  $\pm$  SEM). \* =  $p < 0.05$  and \*\* =  $p < 0.01$  for the difference between enflurane (ES, broken line) and halothane (HS, continuous line) groups.

A slightly longer induction time and a frequent occurrence of apnoea (64%) after endotracheal intubation was found during enflurane anaesthesia, which might have indicated a deeper level of anaesthesia with this agent compared with halothane (group HS). However, reactions to intubation, such as closing of vocal cords or coughing were significantly more common during enflurane (72%) than during halothane anaesthesia (32%;  $p < 0.05$ ), showing that the level of anaesthesia with enflurane was just barely deep enough to allow endotracheal intubation.

### Paper III

In the previous investigations (paper I and II) it was assumed that most of the anomalously shaped QRS complexes were

manifestations of ventricular arrhythmias. Recently several authors have suggested that these usually are aberrantly conducted supraventricular impulses (14,23,37,38). In order to gain further information regarding the nature of these arrhythmias arising during halothane anaesthesia five surface ECG leads and one oesophageal lead were recorded in children undergoing adenoidectomy.

Eleven children developed anomalously shaped QRS complexes, ten of these appeared for the first time during surgery. Nine children had A-V nodal rhythm, either before (eight) or during (one) adenoidectomy. One had ectopic atrial rhythm (Table 4). Five children with A-V nodal rhythm also had episodes with anomalously shaped QRS complexes during surgery, but the two types of arrhythmias were never seen in immediate temporal relation to one another.

Table 4

Electrocardiographic findings in 20 children anaesthetized with halothane for adenoidectomy (III). n= number of patients. Some children had arrhythmias both with normal and anomalous QRS configuration but at different times.

|                                                             | n  |
|-------------------------------------------------------------|----|
| Normal QRS configuration                                    | 10 |
| ectopic atrial rhythm                                       | 1  |
| A-V nodal rhythm                                            | 9  |
| Anomalous QRS configuration                                 | 11 |
| isolated, uniform                                           | 3  |
| uniform, in bigemini                                        | 2  |
| uniform, in pairs                                           | 1  |
| varying shape in bigemini                                   | 2  |
| up to four consecutive anomalous beats with a varying shape | 1  |
| very irregular rhythm                                       | 2  |



Eight children had anomalous QRS complexes either of uniform or of multiform configuration, occurring as single beats or in bigeminy (Table 4). In another child, sequences of up to four consecutive anomalous beats were seen. However, the oesophageal lead was displaced in this child, which made it difficult to locate the P waves. Two children developed a very irregular rhythm with linked multiform QRS complexes and varying R-R intervals at a rate of  $150\text{--}170\text{ min}^{-1}$ .

In these ECG recordings, the shape of the P waves and the P-P intervals remained unchanged when the regular sequence of QRS complexes was disturbed by the appearance of anomalous beats. Also, the anomalous QRS complexes were invariably premature, so that the P-R interval was shortened or the P wave even merged with the QRS complex (Fig. 4). In the two children who developed a very irregular rhythm with runs of multiform QRS complexes, the arrhythmia started with a premature anomalous QRS complex. Therefore, it is improbable that there was an atrial focus for the anomalous beats in any of the patients.

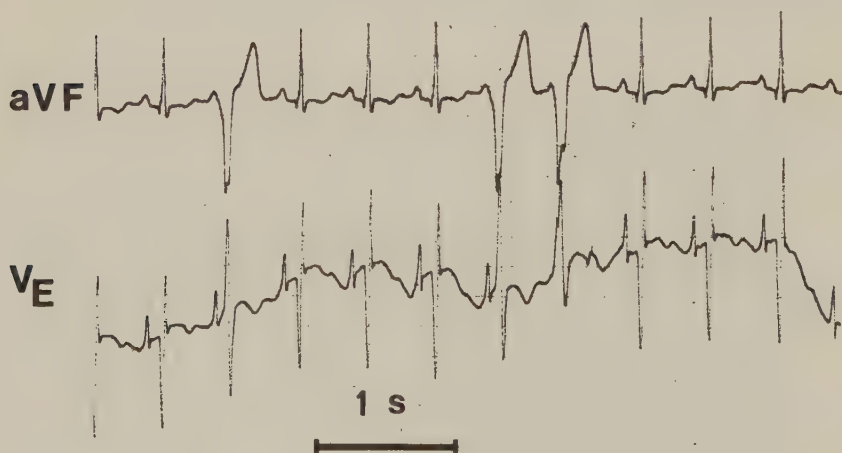


Fig. 4

Boy, 5 yr. Recording during surgery.  $V_E$  is the oesophageal lead. The anomalous QRS complexes are premature and the P waves and the P-P intervals are unchanged.

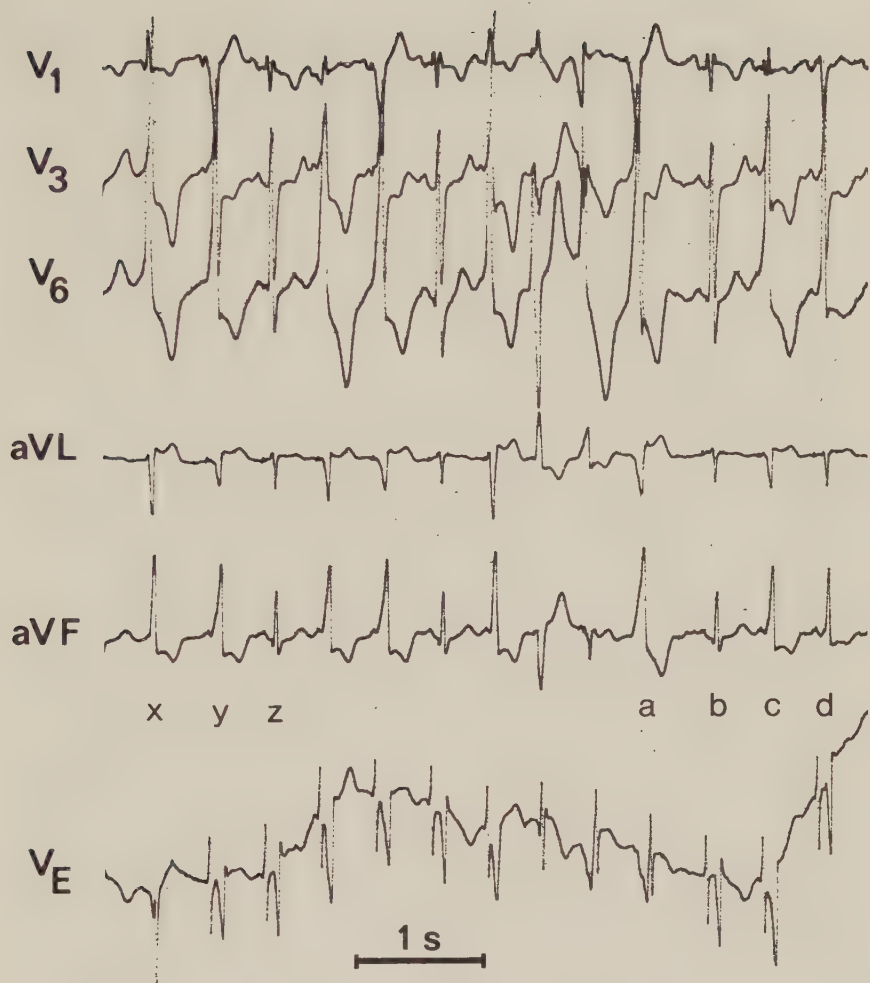


Fig. 5

Girl, 7 yr. Recording during adenoidectomy. A number of beats have been indicated by letters. "b" was regarded as a sinus-evoked beat with normal intra-ventricular conduction. "d" and "c" may be fusion beats. The P wave falls inside the QRS complex of beat "a", which has a shape quite different from that of beat "b". Beat "a" is thus probably a ventricular ectopic beat. Beat "z" has a normal QRS configuration (like beat "b"), while beat "x" and "y" are anomalously shaped. The distance between "y" and "z" is

shorter than that between "x" and "y". This makes it improbable that "y" is a supraventricular beat with aberrant conduction. In that case the impulse resulting in beat "z" would also have been aberrantly conducted, since the impulse would enter a conducting system, which had had even less time to recover from the preceding beat. Thus "z" must be a ventricular capture beat, the presence of which constitutes a strong evidence that an arrhythmia is ventricular (39).

One possible explanation for the present findings is that the anomalous beats were caused by aberrant conduction of impulses arising in the A-V junction, as proposed by Alexander and Murtagh (23). However, as the shape of the P waves was unchanged, such an interpretation would require the additional assumption that retrograde A-V conduction to the atria was always blocked. Furthermore, in the two children with a very irregular rhythm (Fig. 5) there appeared to be occasional complete ventricular capture beats (beats with normal QRS configuration interrupting a sequence of anomalous beats) and several fusion beats (Fig. 5), which are regarded diagnostic signs of ventricular arrhythmia (39). These findings are difficult to reconcile with the hypothesis that the arrhythmia originated in the A-V junction. Furthermore, the hypothesis would not be consistent with experiments in halothane-anaesthetized dogs by Zink, Sasyniuk and Dresel (40). They induced premature anomalous QRS complexes in bigeminy, by infusing adrenaline i.v. while pacing the atria electrically at a rate of  $150-170 \text{ min}^{-1}$ . The anomalous QRS complexes disappeared in most dogs when the atria was paced at very rapid rates. This would hardly have happened if the anomalous beats had an atrial or A-V junctional focus conducted with aberration. Smith and Dresel (41) used a similar technique for provoking anomalous beats during halothane anaesthesia in dogs. By the use of intracardiac electrodes they concluded that the anomalous beats arose in the interventricular septum.

It was concluded that the anomalous QRS complexes found in this study and probably also those of the previous studies (paper I and II) were manifestations of ventricular arrhythmia.

#### Paper IV

The high incidence of ventricular arrhythmias found in previous investigations during halothane anaesthesia (paper I and II) may to some extent be caused by a high stress response to surgery. The influence of premedication on preoperative sedation and the endocrine response to surgical stimuli as reflected by plasma concentrations of ACTH and cortisol were therefore studied. Group A received diazepam  $0.25 \text{ mg kg}^{-1}$  and atropine  $0.015 \text{ mg kg}^{-1}$  (DA) and group B received diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$  (DMH).

The children premedicated with diazepam, morphine and hyoscine (DMH; group B) appeared to be better sedated preoperatively. They also had significantly lower plasma concentrations of ACTH and cortisol, during undisturbed anaesthesia as well as after surgery, than those who received diazepam and atropine (DA; group A). This might to some extent be explained by decreased preoperative anxiety. However, in comparison with initial plasma levels of ACTH and cortisol (found during undisturbed anaesthesia) the postoperative levels had increased less in group B than in group A, which cannot be explained by decreased preoperative anxiety alone. The suppressed ACTH and cortisol response found in group B might be caused by the morphine. But, the doses of morphine were small compared with those ( $1\text{--}4 \text{ mg kg}^{-1}$ ), which have been shown to block ACTH and cortisol response to surgery and stress (42,43,44). Another explanation may be the higher dose of diazepam used in group B, since the sedative effect of this drug is dose dependent (45,46). In addition hyoscine has a greater sedative effect than atropine in the doses used in this investigation, which probably adds to the effects of morphine and diazepam (47).

## Paper V

Previous studies (paper I and II) showed a higher incidence of ventricular arrhythmias during halothane than during enflurane anaesthesia. This did not appear to be due to difference in anaesthetic depth or gas exchange. It was therefore of interest to know whether there was a difference in catecholamine and endocrine response between these two anaesthetic agents.

During undisturbed anaesthesia the plasma catecholamines were significantly higher in the two groups anaesthetized with halothane (HN and HI) as compared with in the groups anaesthetized with enflurane (EN and EI;  $p < 0.05$ ; Fig. 6a and 6b). This finding is in agreement with the results of Joyce and co-workers (48) who found increased noradrenaline release during inhalational induction with halothane in healthy adults. They also found increased noradrenaline concentrations in cat spleen effluent, when the spleen was perfused with halothane. On the other hand, if the excitational stage was circumvented by intravenous induction with thiopentone, before halothane was added, catecholamine release could be prevented (49). Comparative studies on halothane and enflurane have not been done before, but in vivo (50) as well as in vitro (51) studies of enflurane have shown decreased catecholamine secretion from the adrenal medulla. These clinical and experimental results indicate that the agents affect catecholamine release differently during inhalational induction in children.

Immediately after surgery there was a marked increase in plasma catecholamines in the halothane groups, while no significant change occurred in the enflurane groups (Fig. 6a and 6b). The difference in mean values between the agents was also at this stage statistically significant ( $p < 0.001$  for groups HN and EN and  $p < 0.01$  for groups HI and EI). At this stage there was no difference in catecholamine response between non-intubated and intubated children anaesthetized with the same anaesthetic agent neither between group HN and HI nor between group EN and EI (Fig. 6a and 6b). This in spite of the fact that no anaesthesia was given for 2-3 min during surgery (prior to the blood sample)



in the non-intubated children (group HN and EN), while those who were intubated received anaesthesia during the whole procedure (group HI and EI). Thus the catecholamine response to adenoidectomy in children seems to be more dependent upon the choice of anaesthetic agent than the anaesthetic technique or the depth of anaesthesia.

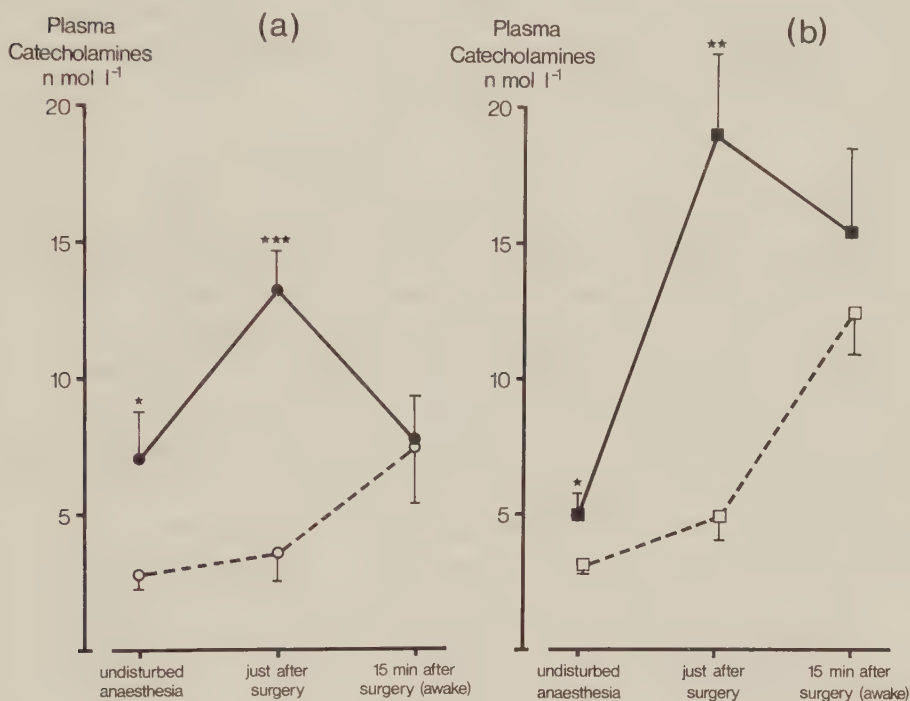


Fig. 6

Mean values  $\pm$  SEM for plasma concentrations of catecholamines at the stages investigated (V)

- a) in non-intubated children during halothane (filled circles, solid line) and enflurane anaesthesia (open circles, dotted line)
- b) in intubated children during halothane (filled squares, solid line) and enflurane anaesthesia (open squares, dotted line). \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$  for the difference between enflurane and halothane anaesthesia.

That the catecholamine concentrations increased significantly in the enflurane groups and decreased in the halothane groups postoperatively, when the children were awake and crying, also supports the suggestion that enflurane reduces and halothane augments catecholamine response to the stress of anaesthesia and surgery in children.

The difference in catecholamine concentrations between enflurane and halothane anaesthesia found in this study, was correlated to the difference in incidence of ventricular arrhythmias found in the previous studies (paper I and II).

#### Paper VI

Previous studies have shown a correlation between high levels of plasma catecholamines (paper V) and a high incidence of ventricular arrhythmias occurring during halothane anaesthesia for adenoidectomy (paper I and II). It has also been shown (paper IV), that a more sedative premedication (DMH; group B) significantly decreased endocrine response to stress, as reflected by plasma concentrations of ACTH and cortisol, compared with a less sedative premedication (DA; group A). The purpose of the present investigation was therefore to study whether this premedication (DMH) also decreased the catecholamine response, and accordingly the occurrence of ventricular arrhythmias during halothane anaesthesia.

The mean sedative score was significantly higher in group B (DMH) than in group A (DA;  $p < 0.001$ ). During undisturbed anaesthesia there was no difference between the groups in catecholamine concentrations (Fig. 7a), but immediately after surgery and 15 min postoperatively they were significantly higher in group A than in group B ( $p < 0.01$  and  $p < 0.05$ , respectively; Fig. 7a). The mean plasma concentrations of ACTH, cortisol and 17- $\alpha$ -hydroxyprogesterone were higher in group A than in group B at all measuring stages (Fig. 7b, 7c and 7d).

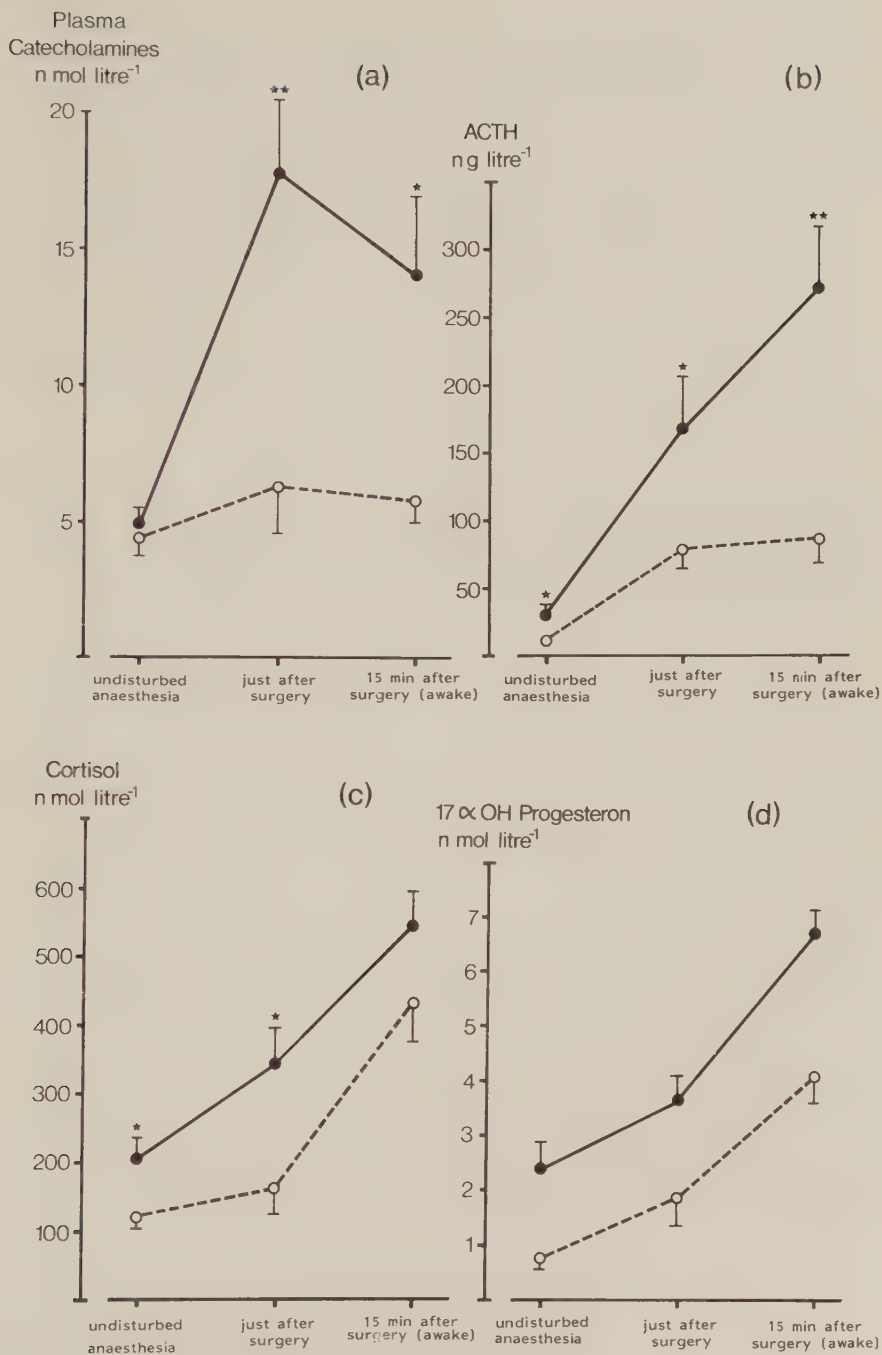


Fig. 7

Mean values  $\pm$  SEM for plasma concentrations of cate-

cholamines (a), ACTH (b), cortisol (c) and 17- $\alpha$ -hydroxyprogesterone (d) for group A (n = 9; continuous line) and for group B (n = 8; dotted line) (VI). \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$ , for the difference between group A and B. Group A was premedicated with diazepam and atropine (DA) and group B was premedicated with diazepam, morphine and hyoscine (DMH).

Table 5

Influence of premedication on cardiac arrhythmias in intubated and spontaneously breathing children during halothane anaesthesia for adenoidectomy (VI). The two groups, A and B, were comparable except for the premedication used.

| Groups                         | HALOTHANE |     |
|--------------------------------|-----------|-----|
|                                | A         | B   |
| Premedications                 | DA        | DMH |
| No. of patients                | 40        | 40  |
| Arrhythmias total %            | 65        | 45  |
| Supraventricular arrhythmias % | 48        | 43  |
| Ventricular arrhythmias %      | 20*       | 3   |
| unifocal VES %                 | 5         | 3   |
| multifocal VES %               | 5         | 0   |
| ventricular tachycardia %      | 10        | 0   |

DA = diazepam about  $0.25 \text{ mg kg}^{-1}$  and atropine about  $0.015 \text{ mg kg}^{-1}$   
DMH = diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$ . \* =  $p < 0.05$  for the difference between group A and B.

The incidence and classification of cardiac arrhythmias is shown in Table 5. Eight children in group A (20%) and only one child in group B (3%) developed ventricular arrhythmia ( $p < 0.05$ ). Two of the children in group A had multifocal ventricular ectopic beats and four developed episodes of ventricular tachycardia,

with a heart rate of  $140-200 \text{ min}^{-1}$ . These arrhythmias occurred during or shortly after surgery, when plasma concentrations of catecholamines were increased by more than 300%. In group B (DMH), however, only one child developed ventricular arrhythmia (isolated unifocal ventricular ectopic beats). In this group plasma catecholamines remained unchanged during surgery. The child who developed ventricular arrhythmia in this group received its premedication 130 min before induction of anaesthesia. This arrhythmia may well have occurred due to a decreased protective effect of the premedication since diazepam and morphine were probably both in the redistribution phase (52,53).

The advantages of the more sedative premedication, in reducing the occurrence of ventricular arrhythmias during these short surgical procedures, were not complicated by a too heavy postoperative sedation. No child had any postoperative airway problems. This premedication has during the last two years been used in more than 500 children subjected to adenoidectomy, without any postoperative airway complications. Furthermore, Haq and Dundee (54) have shown a correlation between preoperative anxiety and increased bleeding in children undergoing adenotonsillectomy, emphasizing the importance of an adequate premedication for these operations.

The two groups investigated in this study were comparable in all respects except for the premedication. It was concluded that for this duration of surgery and degree of surgical stimulation, premedication with a rectal solution of diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$  effectively reduced the incidence of ventricular arrhythmias during halothane anaesthesia. This was due to reduced sympathetic activity found immediately after surgery. The additive central nervous effects of these drugs, on preoperative sedation and on afferent impulses from the surgical field (46,55-58,47), probably account for the clear cut differences in sympathetic and endocrine response demonstrated in this study.



## GENERAL DISCUSSION

The main object of this investigation was to gain more knowledge about the mechanism of ventricular arrhythmias occurring in children during inhalational anaesthesia. Adenoidectomy is a common and standardized surgical procedure, which made it suitable for this investigation. Neither the indications for operation nor the preoperative parental information were changed during the study. All children were out-patients. The operations were performed between 8.30 and 10.30 a.m. in the same operating theatre. One of the parents was present during induction of anaesthesia. The anaesthesia was always conducted by the same anaesthetist (GHS) according to a standardized technique.

There was a significantly higher incidence of ventricular arrhythmias during halothane (41%) than during enflurane (3%) anaesthesia in non-intubated children (paper I). During intubation anaesthesia (paper II) the incidence was reduced to 20% with halothane, which however still was higher than with enflurane (8%).

The high incidence of ventricular arrhythmias during halothane anaesthesia was correlated with high plasma catecholamine levels measured immediately after surgery, while the low incidence of arrhythmias with enflurane was correlated with low plasma catecholamine levels (Fig. 8; paper V). But, there was no significant difference in ACTH or cortisol levels between the two agents. These findings suggest, that the anaesthetics mainly influenced catecholamine release directly, rather than through effects on the central nervous system. Thus, the occurrence of arrhythmias was correlated to plasma catecholamine levels with both anaesthetic agents, but did not seem to be related to the endocrine stress response as reflected by ACTH and cortisol levels.

The catecholamine response was similar in intubated (continued supply of anaesthetics) and in non-intubated (discontinued supply of anaesthetics) children during halothane as well as during enflurane anaesthesia (paper V). Hence, the catecholamine

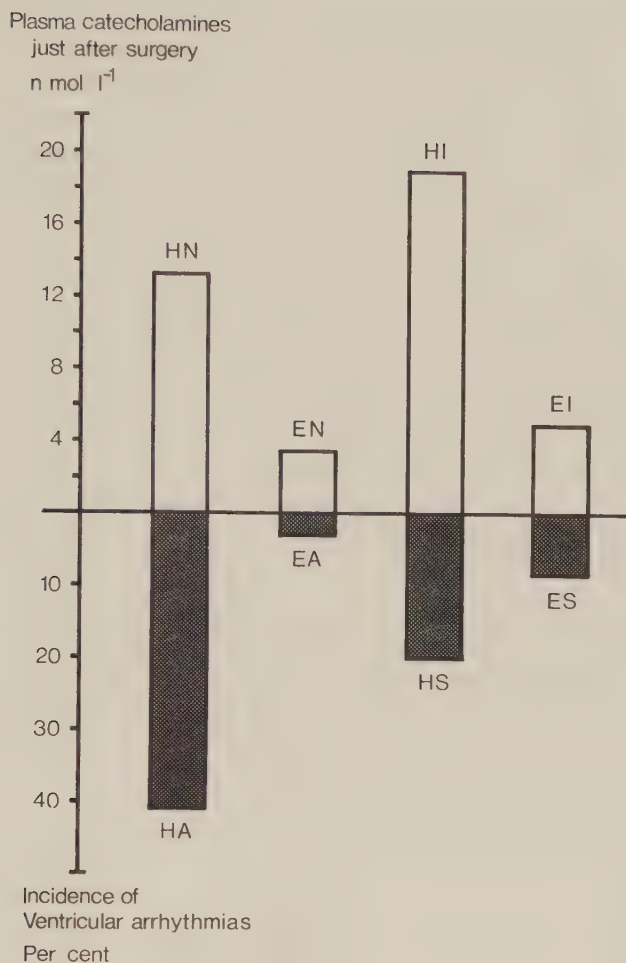


Fig. 8

The mean plasma catecholamine concentrations (white columns) in the four groups studied in paper V related to the incidence of ventricular arrhythmias (shaded columns) in four comparable groups studied in paper I and II. All groups were premedicated with diazepam and atropine (DA) and were breathing spontaneously during the procedure.

HN (V) = HA (I): Halothane anaesthesia, non-intubation

EN (V) = EA (I): Enflurane anaesthesia, non-intubation

HI (V) = HS (II): Halothane anaesthesia, intubation

EI (V) = ES (II): Enflurane anaesthesia, intubation.

response appeared to be more dependent on the choice of anaesthetic agent than on the anaesthetic technique or the depth of anaesthesia. Accordingly, the reduced incidence of ventricular arrhythmias, in intubated, compared with in non-intubated children receiving halothane, was not explained by differences in catecholamine levels. The most logical explanation seems therefore to be related to airways and gas exchange. Although airway obstruction was not frequently observed in the non-intubated group, it may still have occurred. When the airway is not separated from the surgical field by endotracheal intubation a slight airway obstruction may pass unnoticed. The influence of a clear airway and an improved gas exchange, during halothane anaesthesia, was also underlined by a further reduction in the occurrence of ventricular arrhythmias, from 20% to 12%, with manually controlled ventilation (Fig. 9; paper II).

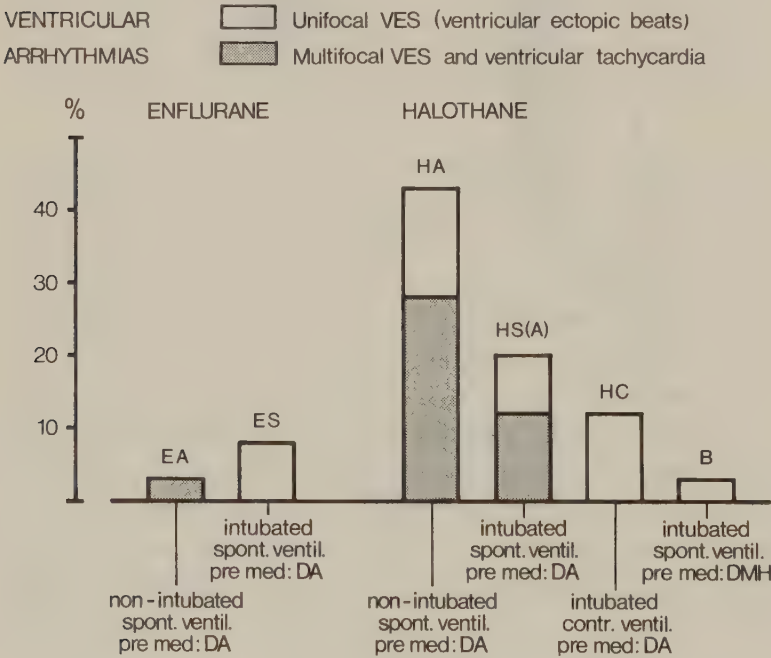


Fig. 9  
Incidence of ventricular arrhythmias in the different groups investigated during enflurane and halothane anaesthesia. DA = diazepam 0.25 mg kg<sup>-1</sup> and atropine 0.015 mg kg<sup>-1</sup>. DMH = diazepam 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>.

Group HS (II) and group A (VI) were identical except for the number of patients investigated (n) and the incidence of ventricular arrhythmias was comparable in the two groups. EA n = 36 (I); HA n = 46 (I); ES n = 25 (II); HS n = 25 (II); HC n = 25 (II); A n = 40 (VI); B n = 40 (VI).

It is well known that endogenous catecholamines and sympathomimetic drugs produce cardiac arrhythmias (59) and that halothane potentiates these effects (6). This was also demonstrated in the present investigation, when the effects of two different premedications on sympathetic and endocrine response were studied (paper VI). The children were intubated in order to avoid the influence of airway obstruction and the two groups were comparable in all respects, except for the premedication used. The more sedative premedication effectively reduced both catecholamine and endocrine response to surgery compared with the less efficient premedication (Fig. 7). Accordingly this was accompanied by a significantly decreased incidence of ventricular arrhythmias, from 20% (group A) to less than 3% (group B; Fig. 9). This demonstrated the central role of catecholamines in the development of ventricular arrhythmias during halothane anaesthesia found in this investigation.

## CONCLUSION

This investigation showed that:

- \* the incidence of ventricular arrhythmias was significantly higher with halothane than with enflurane anaesthesia,
- \* the incidence of ventricular arrhythmias was lower in intubated than in non-intubated children anaesthetized with halothane and the incidence was further decreased by manually controlled ventilation,
- \* widened QRS complexes occurring during halothane anaesthesia are usually manifestations of ventricular arrhythmias,
- \* a rectal premedication with diazepam, morphine and hyoscine significantly decreased plasma ACTH and cortisol response to surgery during halothane anaesthesia,
- \* plasma catecholamines were significantly higher during halothane than during enflurane anaesthesia,
- \* a rectal premedication with diazepam, morphine and hyoscine significantly decreased catecholamine response to surgery and prevented the occurrence of ventricular arrhythmias during halothane anaesthesia.



## CLINICAL CONSIDERATIONS

The present investigation showed that the incidence of potentially dangerous arrhythmias was high in non-intubated children anaesthetized with halothane for adenoidectomy. These arrhythmias were markedly reduced by endotracheal intubation and controlled ventilation. When an efficient premedication was used the occurrence of ventricular arrhythmias was nearly eliminated (Fig. 9). Thus, using inhalational induction with halothane for adenoidectomy an efficient premedication, intubation and controlled ventilation is recommended.

During enflurane anaesthesia the incidence of ventricular arrhythmias was low irrespective of the anaesthetic technique or the premedication used. But respiratory depression was more pronounced with enflurane than with halothane, particularly at the anaesthetic depth needed for adenoidectomy. Thus, when enflurane is to be used for adenoidectomy in children, intubation anaesthesia with controlled ventilation would be preferred, also with this agent.

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# Cardiac Arrhythmias in Non-intubated Children during Adenoidectomy. A Comparison between Enflurane and Halothane Anaesthesia

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The incidence of cardiac arrhythmias, heart rate, blood pressure, capillary perfusion and end-tidal CO<sub>2</sub> tension were studied in 167 healthy children 1-12 years of age undergoing adenoidectomy (n=82) and myringotomy (n=85) during enflurane and halothane anaesthesia. The incidence of cardiac arrhythmias was significantly lower during myringotomy than during adenoidectomy. In children undergoing adenoidectomy the incidence of arrhythmias was 38.9% during enflurane anaesthesia and 86.6% during halothane anaesthesia ( $P<0.001$ ). In the halothane group ventricular arrhythmias were observed in 19 patients (41.3%) but only in one child (2.8%) in the enflurane group. The ventricular arrhythmias seen during halothane anaesthesia were unifocal in six patients and multifocal in five and classified as ventricular tachycardia in eight children. Heart rate was increased by about 40% at the onset of ventricular arrhythmias. The heart rate remained unchanged with enflurane anaesthesia during surgery, which may reflect a decreased sympathomimetic activity. It is suggested that the low incidence of ventricular arrhythmias during enflurane anaesthesia may be explained by the combination of a reduced sympathomimetic activity and a lowered susceptibility of the myocardium to the actions of endogenous catecholamines.

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Key words: Adenoidectomy; arrhythmia; children; enflurane; halothane.

The incidence of cardiac arrhythmias is known to be high during surgical procedures in the mouth and throat (1, 2, 3). The clinical significance of cardiac arrhythmias during anaesthesia has, however, been debated for some years (4, 5, 6). Tomlin (7), in an analysis of 48 deaths occurring during dental anaesthesia, suggested that about one-third were associated with circulatory disturbance and Weigard (8) reported seven cases of cardiac arrest among almost 3000 patients undergoing tonsillectomy and/or adenoidectomy.

The aetiology of cardiac arrhythmias during inhalation anaesthesia has been related to a variety of factors such as hypoxia after airway obstruction, hypercarbia, light anaesthesia, surgery in sensitive reflex areas, different anaesthetic agents and the anaesthetic technique used (9, 10, 11, 12, 13).

The purpose of this study was to investigate the incidence of cardiac arrhythmias, to classify them and to compare their occurrence during enflurane and halothane anaesthesia in non-intubated children during myringotomy and adenoidectomy.

## MATERIAL AND METHODS

Eighty-two children undergoing adenoidectomy were randomly divided into two groups, receiving either halothane (group HA, n=46) or

enflurane anaesthesia (group EA, n=36). A control group of 85 children undergoing myringotomy, randomly received either halothane (group HM, n=46) or enflurane anaesthesia (group EM, n=39). All children were day-stay cases and belonged to ASA class I. Patient data are presented in Table 1.

The children were premedicated with 5 mg diazepam (Stesolid®) rectally and 0.3-0.4 mg atropine sublingually administered 20-30 min before induction of anaesthesia. While awake, with one of the parents present, electrodes for ECG and thoracic impedance (Siemens-Elema, Stockholm; 14) were fixed onto the chest of the child. A photoelectric transducer (Siemens-Elema, Stockholm; 14) to register capillary pulsation was attached to the distal part of the flexor side of the thumb. A blood pressure cuff of appropriate size for the child was placed around the left arm.

Anaesthesia was induced with 75% N<sub>2</sub>O in O<sub>2</sub> for 40-60 s before halothane or enflurane was added and the O<sub>2</sub>/N<sub>2</sub>O ratio was adjusted to 50%. At intervals of 4-6 breaths, the concentrations of halothane and enflurane were increased by steps of 0.5% and 1.0%, respectively. In the myringotomy groups (HM and EM), anaesthesia was maintained at 1-1.5% halothane or 2-3% enflurane. In the adenoidectomy groups (HA and EA), the anaesthesia was continued to a deeper level, using equipotent inspired concentrations of halothane (maximized to 2.5%) and enflurane (maximized to 5%), until sufficient for adenoidectomy. The head was then tilted downwards, a mouth gag was inserted and adenoidectomy was performed without further supply of anaesthetics. At the end of surgery the mask was put on again for the administration of 100% oxygen.

The smallest close-fitting mask was used and a cuvette for CO<sub>2</sub> analysis (Siemens-Elema 130; 15) was incorporated in the anaesthetic circuit at the mask connection. The anaesthetic gases were administered through a Mapleson D circuit. In order to minimize rebreathing,

Table 1

Patient data and different groups studied.

|                                    | Adenoidectomy |               | Myringotomy   |               |
|------------------------------------|---------------|---------------|---------------|---------------|
|                                    | HA            | EA            | HM            | EM            |
| Volatile anaesthetic               | halothane     | enflurane     | halothane     | enflurane     |
| No. of patients                    | 46            | 36            | 46            | 39            |
| Boys/girls                         | 27/19         | 22/14         | 26/20         | 22/17         |
| Age in years, range                | 1-10          | 2-11          | 1-12          | 1-12          |
| Age in years, mean $\pm$ s.e. mean | 5.5 $\pm$ 0.3 | 5.8 $\pm$ 0.4 | 5.3 $\pm$ 0.4 | 5.1 $\pm$ 0.4 |

the fresh gas flow was 3 times the estimated minute ventilation. ECG, capillary pulsation (CP), thoracic impedance (TI) and end-tidal CO<sub>2</sub> tension (P<sub>ET</sub>CO<sub>2</sub>, kPa) were continuously registered on a recorder (Siemens-Elema, EM81). Heart rate (HR beats min<sup>-1</sup>) and respiratory rate (f breaths min<sup>-1</sup>, bpm) were calculated from ECG recordings and thoracic impedance curves, respectively. Mean blood pressure (MBP mmHg) was measured once a minute with a Dinamap 850 (Applied Medical Research, Tampa, Florida, USA). After induction of sleep, a vein on the extensor side of the hand was cannulated (n=16) for blood sampling and analyses of venous oxygen (PvO<sub>2</sub>) and carbon dioxide (PvCO<sub>2</sub>, kPa) tensions (Radiometer, Copenhagen, Denmark).

The end-tidal CO<sub>2</sub> meter was calibrated with two known test gases with CO<sub>2</sub> concentrations within the measuring range. Due to dispersion of the infrared spectrum by N<sub>2</sub>O, the CO<sub>2</sub> values were corrected with a factor of 0.95 found for 50% N<sub>2</sub>O/O<sub>2</sub>. Rotameters for O<sub>2</sub> and N<sub>2</sub>O as well as vaporizers for halothane (Fluotec Mark III) and enflurane (Enfluretec) were calibrated.

#### ECG criteria

In all groups the ECG was studied before anaesthesia and patients with ventricular ectopic beats (two children) were excluded from the study. Four patients with abnormal supraventricular rhythms and one with pre-excitation were included. However, only new arrhythmias were noted in these cases. Sinus tachycardia (ST) was not classified as arrhythmia. A HR below 60 min<sup>-1</sup> during 5 s or more was used as a criterion for sinus bradycardia (SB). Isolated ectopic beats were only reported when at least three were seen in the same child. Beats with aberrant QRS configuration were considered to be of ventricular origin (VES), unless there was positive evidence for a supraventricular origin. Three or more consecutive beats of ventricular origin were regarded as ventricular tachycardia (VT).

#### Measurements

HR, MBP, CP, f and P<sub>ET</sub>CO<sub>2</sub> were recorded at the following stages:

- (1) Before induction of anaesthesia.
- (2) After induction of sleep (approximately 2.5 min after start of induction).

Table 2

Mean values ( $\pm$  s.e. mean) of induction time, operation time and time for "partial recovery" (see definition in the text) in seconds (s) for the different groups.

|                                       | Group HA         | Group EA         | Group HM         | Group EM         |
|---------------------------------------|------------------|------------------|------------------|------------------|
| Induction time, s                     | 342.3 $\pm$ 24.6 | 338.3 $\pm$ 23.7 | 224.7 $\pm$ 11.0 | 243.5 $\pm$ 13.3 |
| Time for adenoidectomy/myringotomy, s | 125.5 $\pm$ 8.6* | 99.3 $\pm$ 5.5   | 291.3 $\pm$ 20.1 | 274.7 $\pm$ 19.4 |
| "Partial recovery", s                 | 138.6 $\pm$ 8.2  | 136.9 $\pm$ 7.9  | 81.3 $\pm$ 6.8   | 96.6 $\pm$ 6.5   |

\*  $P < 0.05$  for the difference between HA and EA.

- (3) During undisturbed anaesthesia (3.5-4.5 min after start of induction). At this stage blood sample no. 1 was taken.
- (4) Before adenoidectomy/myringotomy.
- (5) During adenoidectomy/myringotomy. In the adenoidectomy groups measurement of P<sub>ET</sub>CO<sub>2</sub> was impossible at this stage.
- (6) After adenoidectomy/myringotomy. Blood sample no. 2 for blood gases was taken.
- (7) At the end of anaesthesia, when the child was breathing normally swallowing and reacting in a lively way to painful stimuli but still not awake, "partial recovery".

#### Statistics

Between-group comparisons were carried out with the two-sided Student's *t*-test and chi-square test. Probability values below 0.05 were considered to indicate statistical significance.

## RESULTS

A slight airway obstruction was noticed in 10-15% of the children in the various groups and moderate laryngospasm was seen in only three cases. The time for induction of anaesthesia and for "partial recovery" was similar in groups HA and EA at equipotent halothane and enflurane concentrations. The time for adenoidectomy was significantly shorter in group EA than in group HA ( $P < 0.05$ , Table 2).

#### Arrhythmias

With both agents, arrhythmias occurred more often during adenoidectomy than during myringotomy (Table 3). In group HA, cardiac arrhythmias were found in 38 of 46 (86.6%) children as compared to 14 of 36 (38.9%) children in group EA (Table 3,  $P < 0.001$ ). In groups HA and EA, arrhythmias were most common during surgery (Fig. 1).

*Supraventricular arrhythmias* were found in 73.9% of the children in group HA and in 36.1% of the children in group EA. Junctional rhythm was most common. Wandering pacemaker, sinus bradycardia and supraventricular ectopic beats were also seen (Table 4).

*Ventricular arrhythmias* occurred almost exclusively in the halothane groups (HA and HM, Table 4). In group HA they were found in 41.3% of the children, as compared to

Table 3

Incidence of cardiac arrhythmias in each group.

|                                       | Groups      |            |            |            |
|---------------------------------------|-------------|------------|------------|------------|
|                                       | HA<br>n=46  | EA<br>n=36 | HM<br>n=46 | EM<br>n=39 |
| Total no. of patients with arrhythmia | 38 (86.6%)* | 14 (38.9%) | 15 (32.6%) | 4 (10.3%)  |
| Supraventricular arrhythmias          | 34 (73.9%)* | 13 (36.1%) | 10 (21.7%) | 4 (10.3%)  |
| Ventricular arrhythmias               | 19 (41.3%)* | 1 (2.8%)   | 5 (10.9%)  | 0          |

\*\*\*  $P<0.001$  and \*  $P<0.05$  for the differences between groups HA and EA.

2.8% in group EA ( $P<0.05$ ). Most ventricular arrhythmias in the HA group occurred during surgery (Fig. 2). Unifocal VES was seen in six cases, five developed multifocal VES and eight had ventricular tachycardia. Two children developed a chaotic ventricular rhythm with a ventricular rate of about  $220 \text{ min}^{-1}$ . Circulatory symptoms such as weak peripheral pulses and general paleness were noticed, and illustrated by a decreased capillary pulsation (Fig. 3).

#### Heart rate, blood pressure and capillary pulsation

From stage 1 to stage 7, HR increased by 24% in group HA and by 34% in group EA (Fig. 4a,  $P<0.05$ ). Before adenoidectomy (stage 4) HR was significantly higher in group EA than in group HA (Fig. 4a,  $P<0.001$ ). During and just after surgery (stages 5 and 6) HR increased significantly in group HA ( $P<0.05$ ), while it remained almost unchanged in group EA. There was no significant difference in MBP (Fig. 4b) or CP between the adenoidectomy groups.

#### Respiratory rate and end-tidal carbon dioxide tension

In children anaesthetized with halothane, the respiratory rate (mean  $\pm$  s.e. mean) for stages 2–5 was significantly increased as compared to the preanaesthetic rate ( $P<0.01$ , Fig. 5a). The respiratory rate was, however, unchanged in the children receiving enflurane anaesthesia.

In group HA,  $P_{\text{ETCO}_2}$  (mean  $\pm$  s.e. mean) increased from  $5.1 \pm 0.3 \text{ kPa}$  before anaesthesia to a maximum of  $5.8 \pm 0.3 \text{ kPa}$  after adenoidectomy (n.s.). The corresponding increase in group EA was from  $5.2 \pm 0.2 \text{ kPa}$  to  $7.3 \pm 0.3 \text{ kPa}$  ( $P<0.01$ ). The difference between the

NO. OF CHILDREN WITH ARRHYTHMIAS

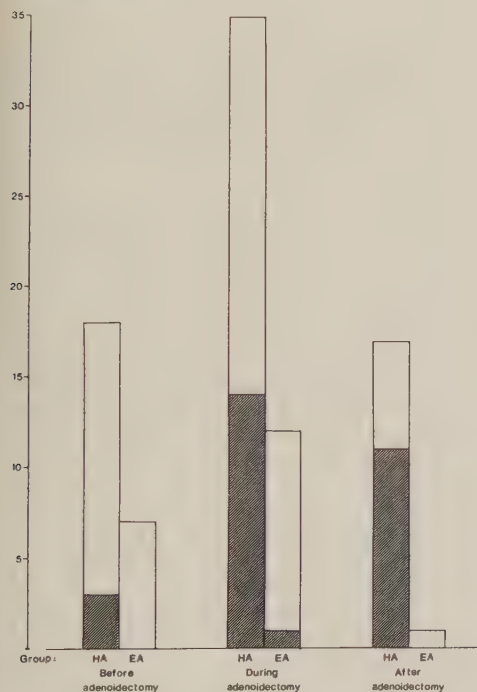


Fig. 1. Arrhythmias in the adenoidectomy groups (HA and EA) are shown before, during and after adenoidectomy. Shaded areas indicate ventricular and white areas supraventricular arrhythmias.

Table 4

Classification of arrhythmias in each group. Note the high incidence of multifocal VES and VT in groups HA and HM.

|                                              | HA<br>n=46 | EA<br>n=36 | HM<br>n=46 | EM<br>n=39 |
|----------------------------------------------|------------|------------|------------|------------|
| Supraventricular arrhythmias                 | 34         | 13         | 10         | 4          |
| Sinus bradycardia                            | 4          | 2          | 1          | 1          |
| Supraventricular extrasystole                | 4          |            | 1          | 1          |
| Wandering atrial pacemaker                   | 6          | 2          |            |            |
| Paroxysmal atrial tachycardia                |            | 1          |            |            |
| Junctional rhythm                            | 30         | 10         | 10         | 2          |
| Aberrant conduction                          | 1          |            |            |            |
| Ventricular arrhythmias                      | 19         | 1          | 5          | 0          |
| Single VES or VES in bigeminy with one focus | 6          |            | 1          |            |
| Multifocal VES                               | 5          |            | 3          |            |
| Ventricular tachycardia (VT)                 | 8          | 1          | 1          |            |

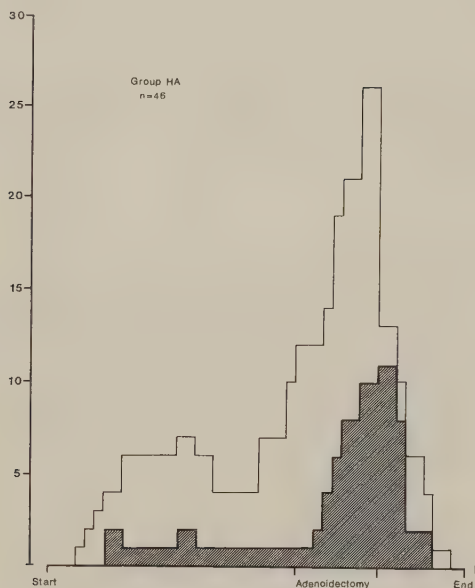
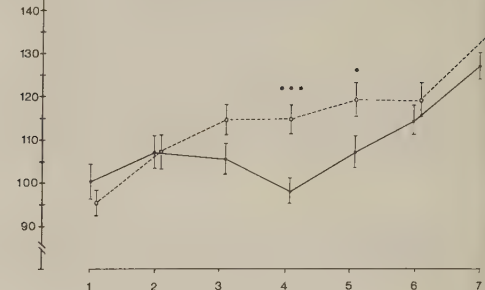
NO. OF CHILDREN WITH  
ARRHYTHMIA

Fig. 2. The occurrence of arrhythmias related to anaesthesia and surgery. The shaded area demonstrates ventricular and the white area supraventricular arrhythmias.

HEART RATE

beats  $\text{min}^{-1}$ 

MBP

mmHg

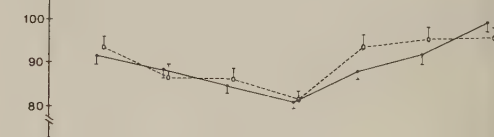


Fig. 4. Mean values ( $\pm$ s.e.mean) for heart rate (a) and mean blood pressure, MBP, (b) at different stages of the procedure in children anaesthetized with enflurane (broken line) and with halothane (continuous line) for adenoidectomy. \*\*\* =  $P < 0.001$  and \* =  $P < 0.05$  for the difference between enflurane and halothane groups.

highest values in the two groups was significant ( $P < 0.05$ , Fig. 5b). There was no statistically significant increase in  $P_{\text{ETCO}_2}$  during myringotomy in either group. Venous blood gases in group HA and EA are shown in Table 5.

## DISCUSSION

The tilted head technique for adenoidectomy in non-intubated children carries the risk of airway obstruction, with concomitant hypoxia and hypercarbia, two factors

which are both known to increase the incidence of ventricular arrhythmias during anaesthesia (10, 11). In the present study, however, airway obstruction was noted in only 10–15% of the children in the various groups and occurred mostly during the induction of anaesthesia. On the other hand, arrhythmias were most common during surgery (Fig. 1). Furthermore, analysis of venous blood gases in 16 patients did not reveal any hypoxia. End-tidal  $\text{CO}_2$  tensions as high as 8 kPa were measured in some patients anaesthetized with enflurane. This was not the reason for the high incidence of



Fig. 3. Capillary pulsation (CP), respiratory rate (f) and ECG in one child with sinus rhythm and with a chaotic ventricular arrhythmia. Note the decreased CP during arrhythmia.

Table 5

Mean values ( $\pm$ s.e.mean) for  $P_{\text{VO}_2}$  and  $P_{\text{VCO}_2}$  in kPa for each group at stage 3 and at stage 6.

|                                      |                    | Group HA<br>n=8    | Group EA<br>n=8 |
|--------------------------------------|--------------------|--------------------|-----------------|
| Undisturbed<br>anaesthesia (stage 3) | $P_{\text{VO}_2}$  | $20.3 \pm 1.7$     | $17.4 \pm 1.6$  |
|                                      | $P_{\text{VCO}_2}$ | $6.2 \pm 0.5$      | $6.4 \pm 0.2$   |
| After adenoidectomy<br>(stage 6)     | $P_{\text{VO}_2}$  | $9.7 \pm 0.8^{**}$ | $7.2 \pm 0.5$   |
|                                      | $P_{\text{VCO}_2}$ | $6.2 \pm 0.4^*$    | $7.3 \pm 0.3$   |

\*\* =  $P < 0.01$  \* =  $P < 0.05$  for the difference between the groups.



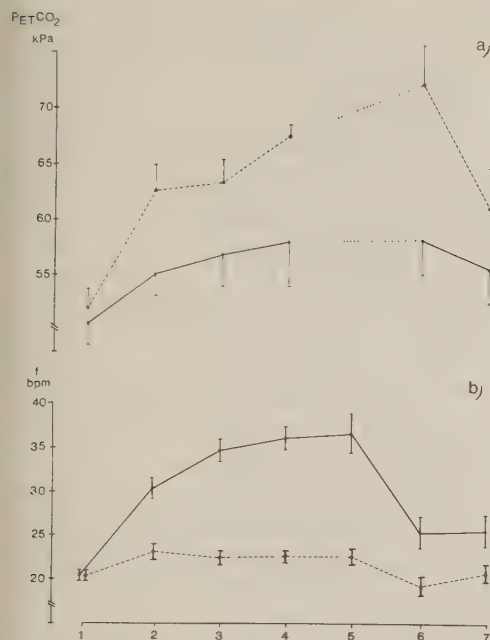


Fig. 5. End-tidal CO<sub>2</sub> tension (P<sub>ET</sub>CO<sub>2</sub>, a) and respiratory rate (f, b) at different stages of the procedure (mean  $\pm$  s.e. mean), in eight children anaesthetized with enflurane (broken line) and with halothane (continuous line) for adenoidectomy. During adenoidectomy (stage 5) P<sub>ET</sub>CO<sub>2</sub> could not be measured (dotted line).

arrhythmias, since arrhythmias were much more common in the halothane group, which had no CO<sub>2</sub> retention.

The anaesthetic technique used in this study also implied a discontinued supply of inhalational anaesthetics during surgery, resulting in a more superficial anaesthesia towards the end of the procedure. As adenoidectomy is performed within a well-innervated area, a continuously lighter anaesthesia during the operation may give a high endogenous stress response. The similarity in induction times with enflurane and halothane anaesthesia would suggest a deeper anaesthetic level with enflurane because of its lower blood/gas partition coefficient as compared to halothane (16). Clinically, however, swallowing and coughing reflexes returned earlier in the enflurane group. This was reflected in the significantly shorter operation time. In fact, an inadequate anaesthetic level in the enflurane group occasionally made it difficult for the surgeon to complete the adenoidectomy (Table 2). In spite of this, the incidence of ventricular arrhythmias was signif-

icantly lower than when halothane was used, a difference also found by Lindgren (17) in children subjected to adeno-tonsillectomy during intubation anaesthesia with controlled ventilation. However, the incidence of cardiac arrhythmias reported by Lindgren was lower than in the present study. This deviation could partly be explained by the intravenous injections of thiopentone and althesin used by Lindgren for the induction of anaesthesia, as both are reported to have protective effects against arrhythmias during oral surgery (18, 19, 20). Furthermore, the intubation technique allows a continuous supply of inhalation anaesthetics and an appropriate depth of anaesthesia could be kept during surgery. This probably results in a lower endogenous stress response and decreased interaction between endogenous catecholamines, myocardium and halogenated anaesthetics (12).

As the operative trauma was similar in both adenoidectomy groups, the high incidence of ventricular arrhythmias during halothane anaesthesia, as compared to enflurane anaesthesia, suggests a higher degree of myocardial sensibilization for endogenous stress hormones. This opinion is supported by experimental and clinical studies on exogenously administered sympathomimetic drugs showing a lower incidence of ventricular arrhythmias during enflurane than during halothane anaesthesia (21, 22, 23). The exact mechanism for the aetiology of ventricular arrhythmias during halothane anaesthesia is, however, not known. Atlee & Alexander (24) observed a slowing of the conductivity in the AV-node as well as in the Purkinje fibres. This might give rise to a re-entry phenomenon (25). Enflurane is also known to retard the conductivity in the AV-node but has no effect on the Purkinje fibres (26). The different effects of the two agents on the Purkinje fibres might constitute an electrophysiological background for the increased myocardial susceptibility with halothane as compared to enflurane anaesthesia.

It is also known that enflurane has a positive and halothane a moderately negative chronotropic heart effect (27, 28, 29). In conformity with this, an increased heart rate before surgery was found in the enflurane group (stages 1-4, Fig. 4a) and no further increase occurred during surgery (stage 5-6). In the halothane group, however, the heart rate remained almost unchanged before surgery, but showed a significant increase during surgery ( $P < 0.05$ , Fig. 4a). In an experimental study, Zink et al. (30) used i.v. infusion of adrenaline during halothane anaesthesia. They found that ventricular arrhythmias did not appear until the heart rate was increased by about 35%. In the present study the mean heart rate for those children ( $n = 19$ ) who developed ventricular arrhythmias during halothane

anaesthesia was increased by almost 40% at the onset of this condition. In children anaesthetized with halothane who did not develop ventricular arrhythmias the heart rate was increased by less than 15% during surgery.

We found it somewhat surprising that heart rate increased less during surgery in children given enflurane than among those given halothane. In fact, the positive chronotropic effect of enflurane should have made the sinus node more susceptible to the stress of surgery. These findings may suggest that sympathetic activity was less in children anaesthetized with enflurane. Perhaps the low incidence of ventricular arrhythmias with enflurane may be explained by the combination of reduced sympathomimetic activity and lowered susceptibility of the myocardium to the actions of endogenous catecholamines.

## ACKNOWLEDGEMENTS

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## II.

### CARDIAC ARRHYTHMIAS IN INTUBATED CHILDREN DURING ADENOIDECTOMY. A COMPARISON BETWEEN ENFLURANE AND HALOTHANE ANAESTHESIA

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In 75 children undergoing adenoidectomy, occurrence of cardiac arrhythmias and influence of anaesthesia on respiration were studied during halothane and enflurane anaesthesia. All the children were intubated orally. In 25 children halothane, and in another 25 children enflurane was used during spontaneous ventilation. Twenty-five children were also followed during halothane anaesthesia with manually controlled ventilation. The overall incidence of cardiac arrhythmias was higher during halothane anaesthesia (72% at spontaneous breathing and 68% with controlled ventilation) than during enflurane anaesthesia (32%,  $p < 0.05$ ). Ventricular arrhythmias were noted in 20% of the spontaneously breathing children and in 12% of those with controlled ventilation during halothane anaesthesia. Three children breathing spontaneously during halothane anaesthesia developed ventricular tachycardia. During enflurane anaesthesia the incidence of ventricular arrhythmias was lower (8%) in spite of higher end-tidal  $\text{CO}_2$  tensions and an anaesthetic depth that was only just the level needed to allow intubation.

The incidence of ventricular arrhythmias during halothane anaesthesia was shown to be influenced by the anaesthetic technique used, which was not found with enflurane anaesthesia. The greater stability in cardiac rhythm with enflurane indicates a more favourable effect of this agent on the myocardium as well as a decreased sympathetic response to anaesthesia and surgery as compared with halothane anaesthesia.

Cardiac arrhythmias during oral surgery are frequently described (1,2,3,4). In a previous study of non-intubated children

undergoing adenoidectomy using the tilted head technique, the incidence of ventricular arrhythmias was significantly higher during halothane than during enflurane anaesthesia (5). With the tilted head technique the supply of anaesthetics is discontinued during surgery resulting in a lighter anaesthesia towards the end of the surgical procedure. This probably gives rise to an increased endogenous catecholamine response which in the presence of halothane is known to elicit ventricular arrhythmias (6,7). Enflurane, on the other hand, is known to have a less sensitizing influence on the myocardium which may be the explanation for the low incidence of ventricular arrhythmias found in connection with this agent (8,9,10,11).

The aim of the present study was to follow the incidence of arrhythmias in intubated children undergoing adenoidectomy with halothane and enflurane anaesthesia. A comparison of induction and recovery times, of breathing pattern, end-tidal carbon dioxide concentrations and of laryngeal reactions to intubation with these two anaesthetic agents was also made.

## MATERIALS AND METHODS

Seventy-five children subjected to adenoidectomy were randomly divided into 3 groups with 25 patients in each. Group HS received halothane and group ES enflurane anaesthesia. In both groups the children were breathing spontaneously. In group HC, halothane was used with manually controlled ventilation. All patients were day-stay cases and were evaluated to be of the ASA class I.

Group HS consisted of 16 boys and 9 girls, 2-11 years old (mean  $4.9 \pm 0.5$ ), group ES of 18 boys and 7 girls, 1-12 years old (mean  $5.1 \pm 0.5$ ) and group HC of 12 boys and 13 girls, 2-11 years old (mean  $5.7 \pm 0.5$ ).

All the children were premedicated with a combination of 5 mg diazepam (Stesolid<sup>R</sup>) rectally and 0.3-0.4 mg atropine sublingually administered 20-30 minutes before induction of anaesthesia.

While awake, with one of the parents present, electrodes for ECG were fixed onto the chest of the child. A photoelectric transducer (Siemens-Eléma, Stockholm; 12) for registration of capillary pulsation was attached to the distal part of the flexor side of the thumb. A blood pressure cuff of appropriate size for the child was placed around the left arm.

Anaesthesia was induced with  $O_2/N_2O$  ( $FiO_2$  0.25) administered for 1 minute before halothane or enflurane was added and the  $O_2/N_2O$  ratio was adjusted to 1:1 ( $FiO_2$  0.5). The concentrations of halothane and enflurane were increased at intervals of 4–6 breaths by steps of 0.5% and 1% respectively to a maximum of 2.5% for halothane and 5% for enflurane. In group HC the ventilation was controlled as soon as  $P_{ET}CO_2$  reached 5.4 kPa. Before intubation all groups were manually ventilated for 15–20 seconds and the oro-tracheal intubation performed without the use of muscle relaxants. A Mapleson D circuit with fresh gas flows of 3 times the estimated minute ventilation was used to minimize re-breathing.

ECG, capillary pulsation (CP), and end-tidal  $CO_2$  tension ( $P_{ET}CO_2$ , kPa) were continuously registered on a recorder (Siemens-Eléma, EM81). Heart rate (HR,  $beats\ min^{-1}$ ) and respiratory rate ( $f$ ,  $breaths\ min^{-1}$ , bpm) were calculated from ECG recordings and end-tidal  $CO_2$  curves, respectively. Systolic and diastolic blood pressures were measured indirectly and the mean blood pressure (MBP) was calculated. After induction of sleep, a vein on the extensor side of the hand was cannulated for blood sampling and analyses of venous oxygen ( $PvO_2$ , kPa) and carbon dioxide ( $PvCO_2$ , kPa) tensions (Radiometer, Copenhagen, Denmark).

The cuvette for  $CO_2$  analysis (Siemens-Eléma 130; 13) was incorporated in the anaesthetic circuit at the mask or tube connection. The end-tidal  $CO_2$  meter was calibrated by 2 known test gases of  $CO_2$  concentrations within the measuring range. Due to dispersion of the infrared spectrum by  $N_2O$ , the  $CO_2$  values were corrected with a factor of 0.95 found for 50%  $N_2O/O_2$ . Calibrated rotameters for  $O_2$  and  $N_2O$  as well as vaporizers for

halothane (Fluotec Mark III) and enflurane (Enfluretec) were used.

### ECG criteria

Sinus tachycardia (ST) was not classified as arrhythmia. A HR below  $60 \text{ min}^{-1}$  during 5 seconds or more was used as a criterion for sinus bradycardia (SB). Isolated ectopic beats were only reported when at least three were seen in the same child. Beats with bizarre QRS configurations were considered to be of ventricular origin (VES), unless there was positive evidence for a supraventricular origin. Three or more consecutive beats of ventricular origin were regarded as ventricular tachycardia (VT).

### Measurements

HR, MBP, CP, f and  $P_{\text{ET}}\text{CO}_2$  were measured at the following stages.

- (1) before induction of anaesthesia
- (2) after induction of sleep (approximately 2.5 minutes after start of induction)
- (3) during undisturbed anaesthesia (3.5–4.5 minutes after start of induction). At this stage blood sample no 1 for blood gases was taken
- (4) before intubation
- (5) after intubation
- (6) during adenoidectomy
- (7) after adenoidectomy. Blood sample no 2 for blood gases was taken
- (8) after extubation, when the child was breathing normally, swallowing and reacting in a lively way to painful stimuli but still not awake, "partial recovery".

### Statistics

Between-group comparisons were carried out with the two-sided Student's t-test and the Chi-square test, using Yates correction. Probability values below 0.05 were considered to indicate statistical significance.

## RESULTS

Only those children who had a normal ECG before anaesthesia were included in the study.

The incidence and classification of arrhythmias are shown in Table 1. Arrhythmias were observed in 18 children (72%) in group HS and in 17 in group HC (68%). During enflurane anaesthesia (group ES) 8 children (32%) developed cardiac arrhythmia which was significantly lower than in groups HS and HC ( $p < 0.05$ , Table 1). Junctional rhythm was the most common arrhythmia in all three groups. There was no statistically significant difference between the groups in incidence of ventricular arrhythmias, but the more serious ones, such as multifocal ventricular ectopic beats (1 child) and ventricular tachycardia (3 children) were only seen in group HS (Table 1). Supraventricular arrhythmias were mostly seen during undisturbed anaesthesia or at the beginning of surgery while ventricular arrhythmias occurred during or shortly after surgery.

Table 1

Classification of arrhythmias in the different groups. Note that multifocal ventricular ectopic beats (VES) and ventricular tachycardia only occurred in group HS.

|                              | SPONTANEOUS<br>VENTILATION |                          | CONTROLLED<br>VENTILATION |
|------------------------------|----------------------------|--------------------------|---------------------------|
|                              | n = 25<br>(ES) Enflurane   | n = 25<br>(HS) Halothane | n = 25<br>(HC) Halothane  |
| Arrhythmias total            | 8 (32%)*                   | 18 (72%)                 | 17 (68%)                  |
| Supraventricular arrhythmias | 6 (24%)*                   | 15 (60%)                 | 14 (56%)                  |
| junctional rhythm            | 6                          | 12                       | 14                        |
| ectopic atrial rhythm        | —                          | 2                        | —                         |
| sinus bradycardia            | —                          | 1                        | —                         |
| Ventricular arrhythmias      | 2 (8%)                     | 5 (20%)                  | 3 (12%)                   |
| unifocal VES                 | 2                          | 1                        | 3                         |
| multifocal VES               | —                          | 1                        | —                         |
| ventricular tachycardia      | —                          | 3                        | —                         |

\* =  $p < 0.05$  for the difference between group ES and HS



The ventricular ectopic beats in groups HC and ES occurred as single beats or in bigeminy and were of a uniform shape (unifocal). The underlying rhythm was sinus rhythm with a rate between  $120$  and  $155 \text{ min}^{-1}$ . These arrhythmias lasted for 15 seconds to 3 minutes. No adverse clinical circulatory signs were seen and capillary pulsation and blood pressure were not significantly disturbed. Of the 5 children who developed ventricular arrhythmia in group HS, 1 had unifocal ventricular ectopic beats and another had multifocal ventricular bigeminy for 3 minutes. Three children in this group had ventricular tachycardia with a rate of  $150$  to  $200 \text{ min}^{-1}$  (Fig. 1). In one of these children the arrhythmia continued for 5 minutes. Peripheral circulation, as measured by capillary pulsation was reduced at the occurrence of periods with several ectopic beats (Fig. 2).

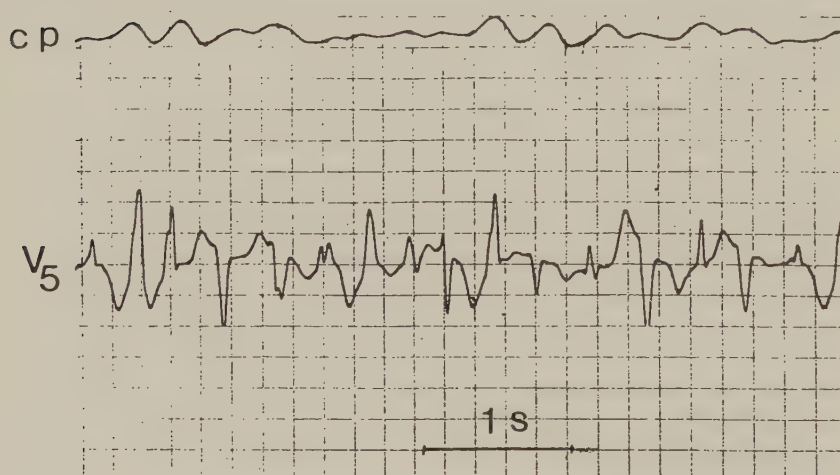


Fig. 1  
ECG (lead  $V_5$ ) and capillary pulsation (CP) in a child anaesthetized with halothane (group HS). Chaotic ventricular rhythm at a rate of  $180 \text{ min}^{-1}$ , started during surgery and lasted more than 3 minutes.

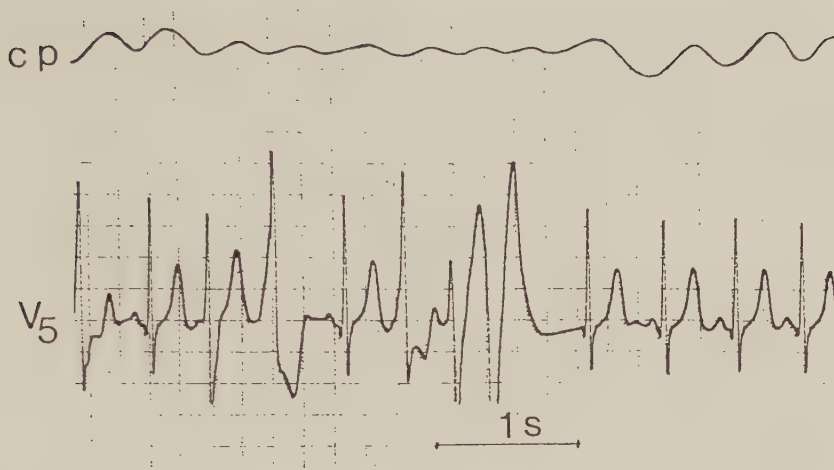


Fig. 2

ECG (lead  $V_5$ ) and capillary pulsation (CP) in a child anaesthetized with halothane (group HS). Note the decrease in amplitude of the capillary pulsation when several ventricular beats occur in succession.

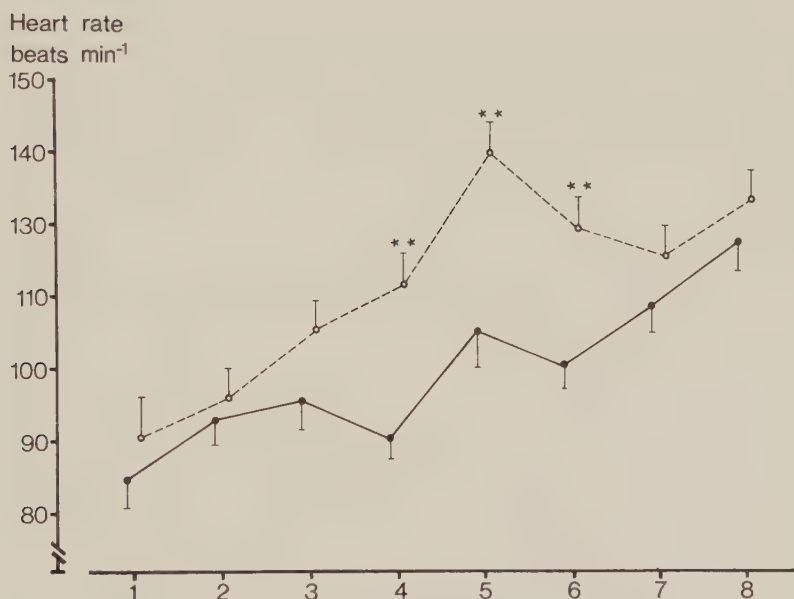


Fig. 3 Mean values ( $\pm$  SEM) for heart rate at different stages of the procedure in children anaesthetized with enflurane (broken line) and with halothane (continuous line). \*\* =  $p < 0.01$  for the difference between enflurane and halothane groups.

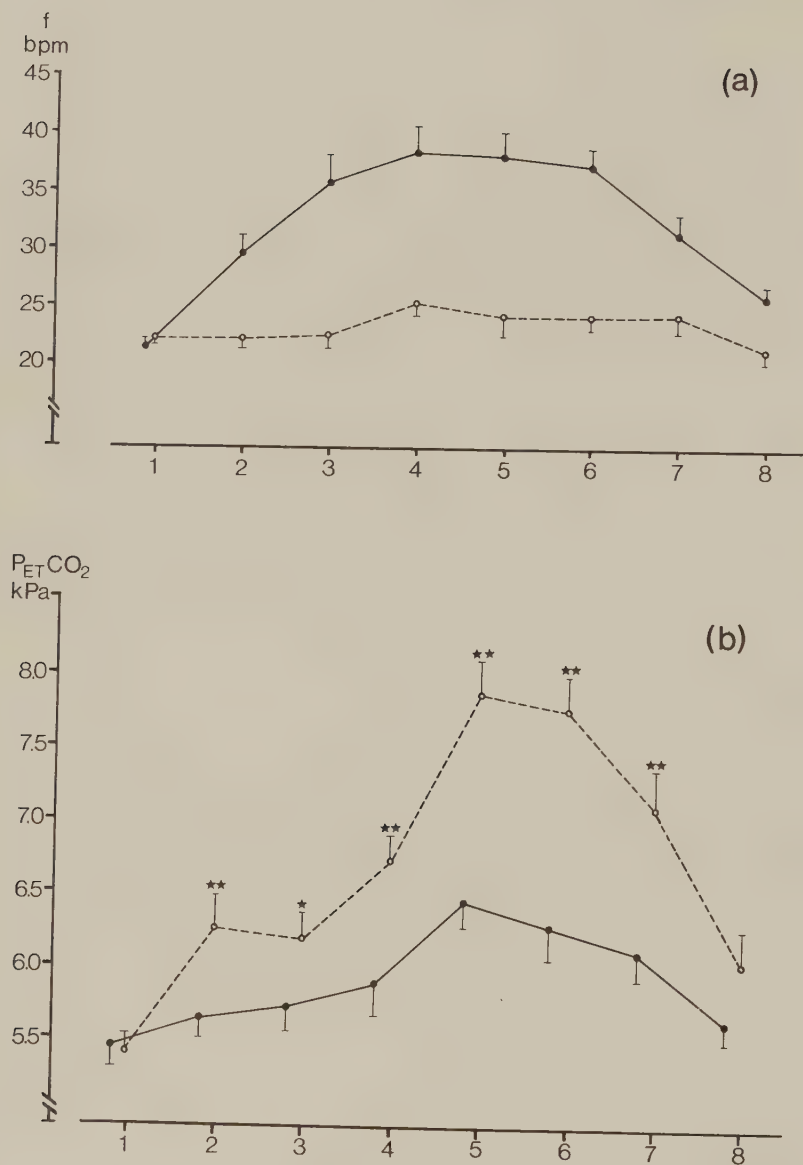


Fig. 4  
Respiratory rate ( $f$ ; a) and end-tidal  $\text{CO}_2$  tension ( $P_{\text{ET}} \text{CO}_2$ ; b) at different stages of the procedure (mean  $\pm$  SEM). \* =  $p < 0.05$  and \*\* =  $p < 0.01$  for the difference between enflurane (ES, broken line) and halothane (HS, continuous line) groups.

During undisturbed anaesthesia the heart rate was significantly increased in group ES (stages 1 to 4), while it remained almost unchanged in group HS (Fig. 3). At intubation (stage 5) there was a similar increase in HR in both groups. At stages 4, 5 and 6 the HR was significantly higher in group ES than in group HS or HC ( $p < 0.01$ , Fig. 1). There was no significant difference in MBP or CP between the groups.

In group HS the respiratory rate during stages 2 to 5 was significantly increased as compared to the preanaesthetic rate ( $p < 0.01$ ). During enflurane anaesthesia the respiratory rate remained unchanged during all stages of the procedure (Fig. 4a). The mean values ( $\pm$  SEM) for  $P_{ET}CO_2$  were significantly increased during anaesthesia and surgery in groups HS and ES. The highest  $P_{ET}CO_2$  levels in groups HS and ES were found after intubation (stage 5). At this stage the mean value ( $\pm$ SEM) in group ES was  $7.9 \pm 0.2$  kPa. Values of 9.3 kPa were found in 2 children. In group HS the mean value ( $\pm$ SEM) at this stage was  $6.5 \pm 0.2$  kPa. In this group the highest  $P_{ET}CO_2$  was 7.7 kPa. At all stages except 1 and 8 (Fig. 4b) the differences in  $P_{ET}CO_2$  between the groups were statistically significant. In group HC the mean values for  $P_{ET}CO_2$  were kept between 5.2 and 5.4 kPa.

Table 2

Mean values ( $\pm$  SEM) for  $PvO_2$  and  $PvCO_2$  in kPa for groups HS and ES at stage 3 and stage 7.

|                                    | n = 14<br>(HS) Halothane | n = 15<br>(ES) Enflurane |
|------------------------------------|--------------------------|--------------------------|
| $PvO_2$                            |                          |                          |
| during undisturbed anaesthesia (3) | $19.0 \pm 0.9$           | $20.5 \pm 1.2$           |
| after adenoidectomy (7)            | $20.0 \pm 1.6$           | $18.1 \pm 1.1$           |
| $PvCO_2$                           |                          |                          |
| during undisturbed anaesthesia (3) | $6.0 \pm 0.2$            | $6.2 \pm 0.2$            |
| after adenoidectomy (7)            | $6.3 \pm 0.2$            | $7.0 \pm 0.2^*$          |

\* =  $p < 0.05$  for the difference between the groups

Venous oxygen tensions were high in all cases, but the mean value of venous CO<sub>2</sub> tension were significantly higher in group ES than in group HS at stage 7 ( $p < 0.05$ ; Table 2).

Table 3

Mean values ( $\pm$  SEM) for induction time (until intubation), operation time and for "partial recovery" (see definition in the text) in seconds (s) for the different groups.

|                             | SPONTANEOUS VENTILATION |                     | CONTROLLED VENTILATION |
|-----------------------------|-------------------------|---------------------|------------------------|
|                             | (ES) Enflurane          | (HS) Halothane      | (HC) Halothane         |
| Time for induction          | 472.4 $\pm$ 28.7 s**    | 423.2 $\pm$ 23.4 s* | 370.5 $\pm$ 14.5       |
| Time for adenoidectomy      | 247.6 $\pm$ 20.8 s      | 248.8 $\pm$ 16.0 s  | 298.8 $\pm$ 28.8       |
| Time for "partial recovery" | 312.6 $\pm$ 17.9 s      | 265.0 $\pm$ 17.9 s  | 299.6 $\pm$ 19.2       |

\* =  $p < 0.05$  for the difference between group HS and HC

\*\* =  $p < 0.01$  for the difference between group ES and HC

Table 4

The occurrence of airway obstruction, reaction to intubation, reaction to extubation and apnoea after intubation in the different groups. Note the high incidence of reaction to intubation and apnoea after intubation in group ES.

| Groups                                                  | n = 25     | n = 25  | n = 25  |
|---------------------------------------------------------|------------|---------|---------|
|                                                         | ES         | HS      | HC      |
| Airway obstruction, total                               | 8 (32%)    | 3 (12%) | 4 (16%) |
| slight (stridulous breathing)                           | 4          | 2       | 2       |
| laryngospasm                                            | 4          | 1       | 2       |
| Reaction to intubation, total                           | 18 (72%)*  | 8 (32%) | 7 (28%) |
| vocal cords not relaxed and/or movements of extremities | 7          | 2       | 3       |
| coughing or "bucking" (after intubation)                | 11         | 6       | 4       |
| Reaction to extubation, coughing                        | 4 (16%)    | 2 (8%)  | 3 (12%) |
| Apnoea after intubation (lasting more than one min)     | 15 (64%)** | 3 (12%) |         |

\* =  $p < 0.05$  and \*\* =  $p < 0.01$  for the difference between group ES and HS



A significantly longer induction time (i.e. the time until intubation) was found in groups ES and HS when compared with group HC ( $p < 0.01$  and  $p < 0.05$  respectively; Table 3). Airway obstruction was noticed in 12-32% of the children in the various groups (Table 4). This occurred mostly during induction of anaesthesia and was always shortlived. Reactions to the endotracheal intubation were significantly more common in group ES than in groups HS and HC ( $p < 0.05$  and  $p < 0.01$ ; Table 4). Apnoea, lasting more than 1 minute, occurring after intubation or after insertion of the mouth-gag was more common and of a longer duration in group ES than in group HS ( $p < 0.01$ ; Table 3). In 6 children anaesthetized with enflurane apnoea lasted more than 5 minutes. It was briefer (less than 2 minutes) in the 3 children in group HS.

## DISCUSSION

In a previous study of non-intubated children undergoing adenoidectomy the incidence of ventricular arrhythmias was 41.3% during halothane and 2.8% during enflurane anaesthesia (5). This anaesthetic technique does not allow a continuous administration of inhalational anaesthetics during the adenoidectomy. It results in a lighter anaesthetic level towards the end of the surgical procedure which may give rise to a high endogenic stress response explaining the frequent arrhythmias found with halothane. In the present study the children were intubated and given anaesthetics throughout the adenoidectomy. The incidence of ventricular arrhythmias during halothane anaesthesia (group HS) was 20% which constituted a reduction of about 50% as compared to results in the previous study cited above (5). Since halothane and catecholamines interact with myocardial rhythmicity (6), the reduction of arrhythmias found in this study may be a reflection of a decreased endogenic stress response due to the continued anaesthesia during surgery. In conformity with our previous results (5) the incidence of cardiac arrhythmias

with enflurane was also in this study found to be low and therefore not particularly influenced by the anaesthetic technique used. This may indicate that there was either a decreased catecholamine response or a less myocardial reactivity when this anaesthetic was used.

The incidence of ventricular arrhythmias with manually controlled ventilation (group HC) was found to be somewhat lower (12%) than with spontaneous breathing (group HS, 20%). Three of these children developed occasional unifocal ventricular ectopic beats during surgery, while multifocal ventricular arrhythmia and ventricular tachycardia were seen in 4 of the children anaesthetized with the same agent breathing spontaneously (group HS). This effect of a controlled mode of ventilation may be due to the differences in carbon dioxide tensions with normocarbica during controlled ventilation and a moderate hypercarbia when the children were breathing spontaneously (Fig. 4). Although these differences were only about 1–1.5 kPa in our study, even small increases in carbon dioxide tensions in connection with surgical stimuli have been shown to be of clinical importance for the development of ventricular arrhythmias during halothane anaesthesia (14, 15).

Earlier experimental studies have shown enflurane to be a more profound respiratory depressant inhalational anaesthetic agent than halothane, with a lowered responsiveness both to hypoxia and hypercarbia (16, 17). Not surprisingly we also found higher  $P_{ET}CO_2$  and  $P_vCO_2$  values in the children anaesthetized with enflurane than with halothane during spontaneous breathing. The incidence of cardiac arrhythmias remained, however, low suggesting that myocardial sensitivity to elevated  $CO_2$  tensions is less with enflurane than with halothane anaesthesia.

As the induction of anaesthesia was standardized as far as possible and since equipotent MAC values for inhaled enflurane and halothane were used, a faster induction time and recovery time would have been expected in the children receiving enflurane, since the solubility of enflurane in blood and tissues is lower than for halothane (18). This was also confirmed by a

more rapid loss of consciousness during enflurane than during halothane anaesthesia. But the induction time i.e. until the anaesthetic level allowed intubation without muscle relaxants was in fact slightly longer with enflurane than with halothane anaesthesia during spontaneous breathing, confirming the observations made by Yakaitis and colleagues in 1979 (19). The frequent occurrence of unrelaxed vocal cords and coughing during intubation with enflurane anaesthesia (Table 4) demonstrated that the anaesthetic level was only just what was needed to allow intubation. Thus, the lower incidence of arrhythmias observed with this agent may not be explained by a too deep anaesthetic level. The stability of the cardiac rhythm with enflurane during adenoidectomy, both in intubated and in non-intubated children may therefore be suggested to depend upon favourable effects of enflurane on the myocardium as well as a decreased sympathetic response to anaesthesia and surgery.

During halothane anaesthesia, however, the incidence of ventricular arrhythmias appeared to be markedly influenced by the anaesthetic technique used, since these were decreased by endotracheal intubation and manually controlled ventilation as compared with in non-intubated children (5). The obvious advantages of securing clear airways, adequate gas-exchange and a maintained level of anaesthesia, seem to be of greater importance for the occurrence of ventricular arrhythmias during halothane, than during enflurane anaesthesia in children undergoing adenoidectomy.

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### III.

#### VENTRICULAR ARRHYTHMIA OR SUPRAVENTRICULAR ARRHYTHMIA WITH ABERRANT CONDUCTION? AN ELECTROCARDIOGRAPHIC STUDY IN HALOTHANE-ANAESTHETIZED CHILDREN UNDERGOING ADENOIDECTOMY

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The ECG was continuously recorded in twenty children undergoing adenoidectomy during halothane anaesthesia. The aim of the study was to identify QRS complexes with an anomalous shape and to determine whether these were aberrantly conducted supraventricular beats or manifestations of ventricular arrhythmia. Five surface ECG leads and an oesophageal lead were used.

In eleven children, there were QRS complexes which had a shape distinctly different from that of the ordinary sinus-evoked beats. Except in one child, these anomalous QRS complexes made their first appearance during surgery, although the arrhythmia continued until 0-1 min after adenoidectomy in some children. The severity ranged from that of occasional anomalous QRS complexes with uniform shape to that of a fast irregular rhythm with a variety of QRS shapes. Although the anomalous QRS complexes were premature, P waves and P-P intervals were unchanged. In some children, there appeared to be ventricular capture beats and fusion beats. Because of this, and in view of evidence gathered from studies in animals, by other authors, we considered it likely that the anomalous beats were ventricular.

QRS complexes with anomalous shapes commonly appear during oral surgery (Kaufman, 1966; Ryder, 1971) particularly with halothane as an anaesthetic. Several authors have suggested that the anomalous QRS complexes usually are aberrantly



conducted supraventricular impulses (Alexander, 1971; Alexander, Bekheit and Fletcher, 1972; Alexander and Murtagh, 1979; Lindgren, 1981).

It has been shown in several animal studies (Hashimoto and Hashimoto, 1972 a and b; Zink, Sasyniuk and Dresel, 1975) that halothane sensitizes the heart to the effects of catecholamines, so that the incidence of ventricular arrhythmia increases. These findings are consistent with the observation by Lindgren (1981) that anomalous QRS complexes are more common during surgery, than during undisturbed anaesthesia. However, the animal studies are difficult to reconcile with the notion that anomalous QRS complexes occurring in halothane anaesthetized patients usually are aberrantly conducted supraventricular beats, rather than manifestations of ventricular arrhythmia.

We knew from previous experience (Sigurdsson et al., 1983) that anomalous QRS complexes are very common, occurring in 41 percent of non-intubated children undergoing adenoidectomy during halothane anaesthesia. However, only one surface ECG lead was used in this study. This made the interpretation of these arrhythmias somewhat uncertain. The differentiation between supraventricular and ventricular arrhythmia often rests on an accurate identification of atrial electric activity. In order to gather further information regarding the nature of arrhythmias arising during halothane anaesthesia we recorded five surface ECG leads and one oesophageal lead continuously in children undergoing adenoidectomy.

## PATIENTS AND METHODS

Twenty children were studied. They underwent adenoidectomy as day-stay cases, were not treated with sympathomimetic drugs and were in good general and cardiac health. Otherwise, no selection of the children was made. They were premedicated 20-30 min before anaesthesia with 5 mg of diazepam rectally and 0.3-0.4 mg of atropine sublingually.

Anaesthesia was induced with 75 percent nitrous oxide in oxygen supplied via a Mapleson D circuit. The fresh gas flow was  $300 \text{ ml kg}^{-1} \text{ min}^{-1}$ . The nitrous oxide concentration was reduced to 50 percent and halothane was added when the child became drowsy. Five surface ECG leads ( $V_1$ ,  $V_3$ ,  $V_6$ , aVL, aVF) were connected when the child no longer reacted to touch. The ECG was written continuously on a Mingograph 81 (Siemens-Elema). The inspired halothane concentration was held at 2.5–3 percent for 3–5 min, with the child breathing spontaneously via a face mask, after which an oesophageal unipolar electrode was inserted with the help of a Macintosh laryngoscope. The electrode consisted of a 60 cm isolated cable, diameter 1.5 mm, and a cylindrical silver tip coated with silver chloride, 3 mm long and 2 mm in diameter. The tip was placed so that the P wave was maximal. The child continued to breathe 2.5–3 percent halothane in nitrous oxide/oxygen until anaesthetic depth was judged sufficient for adenoidectomy. The head was then tilted downwards, a mouth gag inserted and adenoidectomy performed with the non-intubated child breathing air. At the end of surgery, the mouth gag was removed and 100 percent oxygen supplied by mask. The ECG recording ended about 2 min after surgery.

### Terminology

The terms: anomalous QRS complexes or anomalous beats (Bellet, 1972) were used to describe beats where the QRS complex was widened and its shape distinct from that of normally conducted sinus beats. A–V dissociation is an independent action of atria and ventricles, each beating in response to its own pacemaker. The P waves and the QRS complexes have no relation to each other. This condition may arise e.g. during A–V nodal or ventricular tachycardia. Aberrant conduction is used here to describe a functional bundle branch block, where one or more of the bundle branches are refractory when a supraventricular impulse arrives. The shape of the QRS complex becomes widened and often resembles that of a ventricular ectopic beat. Ventricular fusion beat describes a simultaneous stimulation of the ventricles by a supraventricular impulse and an ectopic ventricular impulse. The shape of the QRS complex will be an intermediate between the shape of a normal QRS complex and

that of an ectopic ventricular impulse. This constitutes one of the best diagnostic criteria for the establishment of ventricular ectopic origin (Schamroth, 1980). Ventricular capture beat: in the presence of A-V dissociation, e.g. during ventricular tachycardia, an atrial impulse which occurs during the non-refractory period of both the A-V node and the bundle branches results in a normally conducted QRS complex (the atrial impulse "captures" the ventricles). However, during A-V nodal tachycardia with aberrant conduction, a capturing impulse will also be conducted with aberration, since it is even more premature than the impulses of the basic A-V nodal tachycardia. Thus a normally conducted capture beat constitutes a strong evidence for ventricular rhythm.

Sinus tachycardia or sinus bradycardia were not counted as arrhythmia in this study.

### Statistics

The two-sided Student's t-test for paired data was used.

## RESULTS

Mean age was 6.3 yr (range 3-12 yr). The ECG was recorded during  $7 \pm 4$  min ( $m \pm 1SD$ ) before the mouth gag was inserted. This was held in place for  $3 \pm 1$  min, after which the ECG recording continued for another  $2.1 \pm 0.7$  min.

Eighteen children had a normal sinus rhythm during undisturbed anaesthesia, immediately after connecting the surface ECG leads. The heart rate was  $102 \pm 19 \text{ min}^{-1}$ . The other two had an A-V nodal rhythm (also called A-V junctional by many authors), as diagnosed by normally shaped QRS complexes and P waves which were either absent, or else abnormally shaped and occurring close to or after the QRS complex. Seven other children developed A-V nodal rhythm at a later stage, either before (six) or during adenoidectomy (one). The heart rate at the onset of A-V nodal rhythm was  $96 \pm 17 \text{ min}^{-1}$ . One child had an arrhythmia with variable P waves but normal P-R intervals

before surgery. This was interpreted as an ectopic atrial rhythm. Five of the children with A-V nodal rhythm also had episodes with anomalously shaped QRS complexes during surgery, but the two types of arrhythmia were never seen in immediate temporal relation to one another.

In six children, QRS complexes with an anomalous but uniform shape were seen. In three of these children there were only single anomalous QRS complexes, while they occurred both single and in pairs in one, and both single and in bigeminy, alternating with sinus beats, in two children. A common observation in all six children was that the P-P intervals and the shape of the P waves were unchanged. The anomalous QRS complexes were preceded by shortened P-R intervals, sometimes to the extent that the QRS complex and the P wave coalesced (Fig. 1).

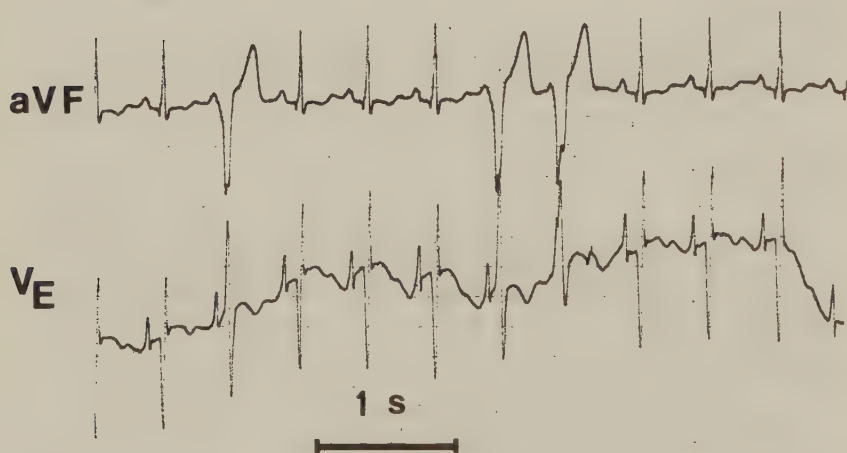


Fig. 1

Boy, 5 yr. Recording during surgery.  $V_E$  is the oesophageal lead.

In two children, anomalous QRS complexes of more than one shape were observed, both single and in bigeminy. The shape of, and intervals between, the P waves were apparently unchanged (Fig. 2). In another child, sequences of up to four

consecutive anomalously shaped QRS complexes were seen during adenoidectomy. The oesophageal lead was displaced in this child. Therefore, it was difficult to locate the P waves.

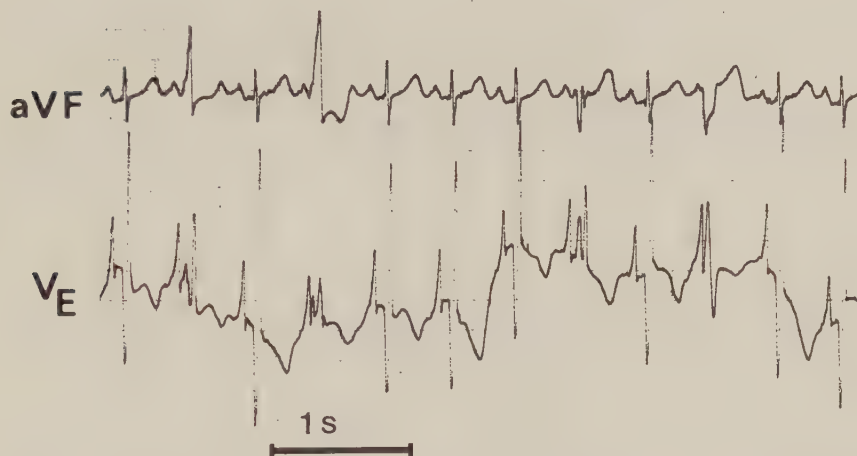


Fig. 2

Boy, 6 yr. Recording during surgery.

In one child, a very irregular rhythm with linked multiform QRS complexes and varying R-R intervals at a rate of  $160\text{--}170\text{ min}^{-1}$  was observed. The arrhythmia started 20 s after insertion of the mouth gag, continued throughout surgery (3 min) but was replaced by sinus rhythm 30 s after removal of the mouth gag. While a variety of QRS shapes were seen, P waves and P-P intervals appeared unaffected (Fig. 3). Several QRS complexes had the appearance of capture beats, i.e. beats with a normal QRS configuration interrupting the sequence of anomalous beats, or ventricular fusion beats. A similar arrhythmia started 3 min after insertion of the mouth gag in another child and continued for 90 s, until about 60 s after removal of the mouth gag (Fig. 4). Sinus rhythm at a rate of  $140\text{ min}^{-1}$  was present just before the onset of the arrhythmia.

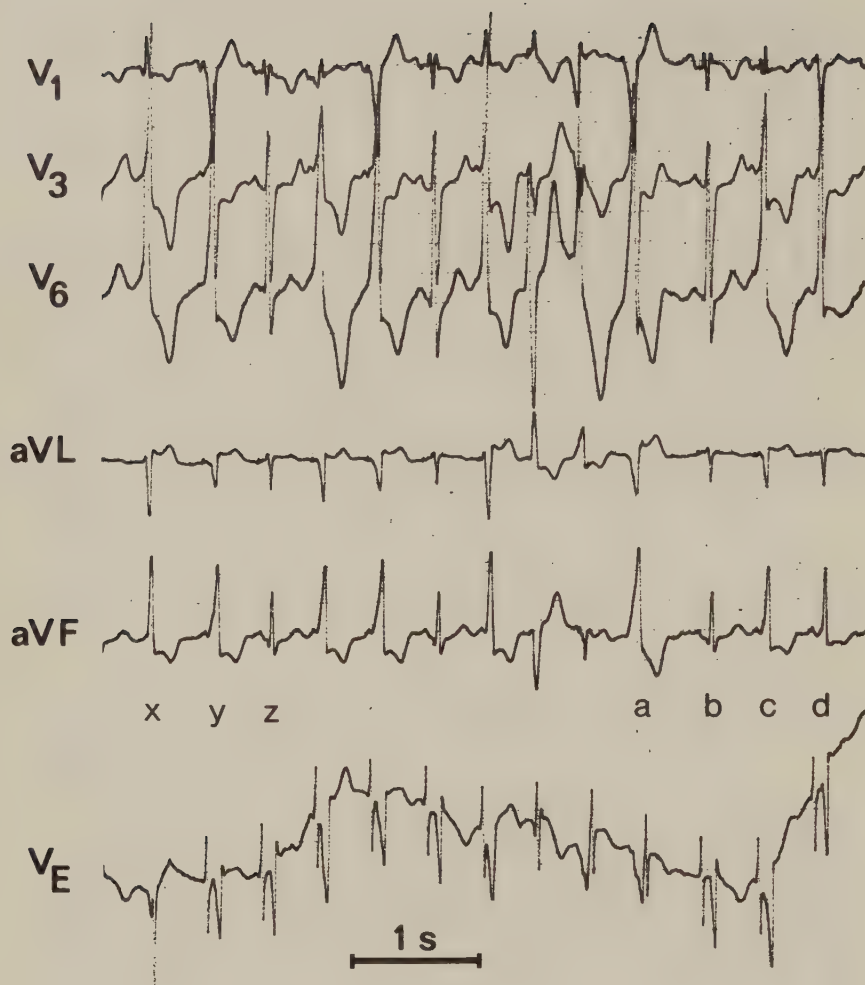


Fig. 3

Girl, 7 yr. Recording during surgery. A number of beats have been indicated by letters. "b" was regarded as a sinus-evoked beat with normal intraventricular conduction. "d" and "c" may be fusion beats. The P wave falls inside the QRS complex of beat "a", which has a shape quite different from that of beat "b". Beat "a" is thus probably a ventricular ectopic beat. Beat "z" has a normal QRS configuration (like beat "b"), while beat "x" and "y" are anomalously shaped. The distance between "y" and "z" is shorter



than that between "x" and "y". This makes it improbable that "y" is a supraventricular beat with aberrant conduction. In that case the impulse resulting in beat "z" would also have been aberrantly conducted, since the impulse would enter a conducting system, which had had even less time to recover from the preceding beat. Thus "z" must be a ventricular capture beat, the presence of which constitutes a strong evidence that an arrhythmia is ventricular (Schamroth, 1980).

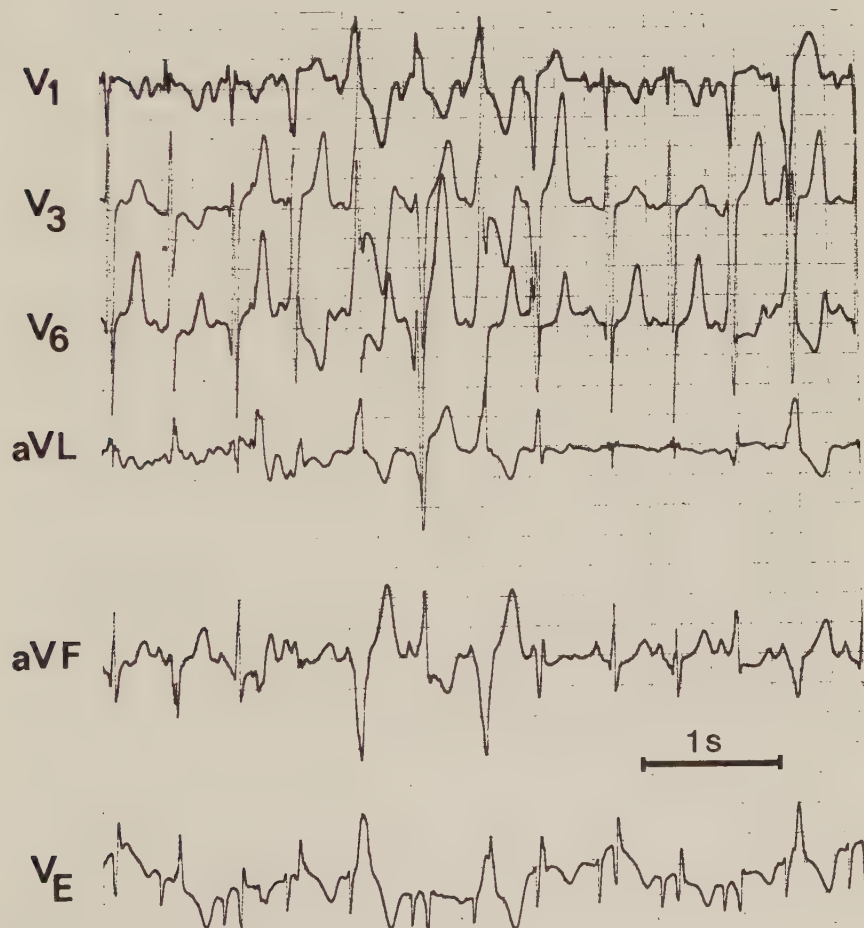


Fig. 4

Boy, 9 yr. Recording during surgery.

Anomalously shaped QRS complexes were thus seen in eleven children (Table). The heart rate was  $133 \pm 17 \text{ min}^{-1}$  when the anomalous beats first occurred as compared to  $102 \pm 16 \text{ min}^{-1}$  at the start of the ECG recording in these children ( $p < 0.001$ ). In one child, anomalous QRS complexes appeared already when the oesophageal electrode was introduced. They reappeared during surgery. In the remaining ten children, the mouth gag was in place at the onset of arrhythmia, although it sometimes ended only after the mouth gag was removed.

Table

Electrocardiographic findings in 20 children anaesthetized with halothane for adenoidectomy. n= number of patients. Some children had arrhythmias both with normal and anomalous QRS configuration, but at different times.

|                                                             | n  |
|-------------------------------------------------------------|----|
| Normal QRS configuration                                    | 10 |
| ectopic atrial rhythm                                       | 1  |
| A-V nodal rhythm                                            | 9  |
| Anomalous QRS configuration                                 | 11 |
| isolated, uniform                                           | 3  |
| uniform, in bigemini                                        | 2  |
| uniform, in pairs                                           | 1  |
| varying shape in bigemini                                   | 2  |
| up to four consecutive anomalous beats with a varying shape | 1  |
| very irregular rhythm                                       | 2  |

## DISCUSSION

In our ECG recordings, P waves and P-P intervals remained unchanged when the regular sequence of QRS complexes was disturbed by the appearance of anomalous beats. Also, anomalous QRS complexes occurring isolated, in pairs, or in bigeminy were invariably premature, so that the P-R interval was

shortened or the P wave even merged with the QRS. In the two children who developed a very irregular rhythm with runs of multiform QRS complexes, the arrhythmia started with a premature anomalous QRS complex. Therefore, it is improbable that there was an atrial focus for the anomalous beats in any of the patients.

One possible explanation for the present findings is that the anomalous beats were caused by aberrant conduction of impulses arising in the A-V junction, as proposed by Alexander and Murtagh (1979). However, as the shape of the P waves was unchanged, such an interpretation would require the additional assumption that retrograde A-V conduction to the atria was always blocked. In the two children with a very irregular rhythm (Fig. 3 and 4) there appeared to be occasional complete ventricular capture beats. Also, there seemed to be several fusion beats (Fig. 3). These findings are difficult to reconcile with the hypothesis that the arrhythmia originated in the A-V junction. Furthermore, the hypothesis would not be consistent with experiments in halothane-anaesthetized dogs by Zink, Sasyniuk and Dresel (1975). They induced premature anomalous QRS complexes in bigeminy, by infusing adrenaline i.v. while pacing the atria electrically at a rate of  $150-170 \text{ min}^{-1}$ . The anomalous QRS complexes disappeared in most dogs when the atria was paced at very rapid rates. This would hardly have happened if the anomalous beats had an atrial or A-V junctional focus conducted with aberration. Smith and Dresel (1982) used a similar technique for provoking anomalous beats during halothane anaesthesia in dogs. By the use of intracardiac electrodes they concluded that the anomalous beats arose in the interventricular septum. In view of these findings, we believe that the arrhythmias with anomalous beats in our patients were also ventricular. One mechanism behind the ventricular arrhythmias may be re-entry, as proposed by Zink and his colleagues. The fact that halothane slows conduction in Purkinje fibres (Atlee and Alexander, 1977) may contribute to a re-entry phenomenon.

There is a certain parallelism between the results of Zink and his colleagues and the present results. Firstly, the anomalous QRS complexes usually appeared for the first time during

surgery. The increased sympathetic discharge at this stage may have cardiac effects, similar to those of adrenaline infusion. Secondly, sinus tachycardia was present when the arrhythmia started, while Zink and co-authors could make premature anomalous beats appear by inducing a moderately increased heart rate through electric pacing of the atria. Alexander and Murtagh (1979) and Lindgren (1981) also found that anomalous beats were more common during surgery, than during undisturbed anaesthesia, although these authors concluded that the anomalous beats were usually caused by impulses arising supraventricularly but with aberrant intraventricular conduction. However, Lindgren (1981) only studied one ECG lead, which may have prevented precise interpretation of the arrhythmias. Therefore, ECG recordings which she suggests show aberrant intraventricular conduction (e.g. Fig. 3 and 4 of her study) might also be interpreted as ventricular arrhythmia. Alexander and Murtagh (1979) used three surface ECG leads. Although they conclude that many of their patients had supraventricular arrhythmia with bundle branch block, the recordings which they reproduce do not exclude the possibility of ventricular dysrhythmia. These comments should not be taken to imply that a firm diagnosis of intermittent bundle branch block during anaesthesia cannot be made from surface ECG leads only. One example to the contrary is given by Edelman and Hurlbert (1980). Another instance, where anomalous QRS complexes might have been caused by aberrant conduction, is provided by Fig. 2 in the paper by Alexander, Bekheit and Fletcher (1972). However, an alternative diagnosis of ventricular tachycardia with retrograde A-V conduction cannot be ruled out in this particular case.

We conclude that the anomalous beats of the present study (Table) most probably were manifestations of ventricular arrhythmia. The high incidence of these beats is consistent with previous electrocardiographic findings in 46 additional children undergoing adenoidectomy, with the same anaesthetic technique (Sigurdsson et al., 1983).

At our hospital this used to be the most common method of anaesthesia for adenoidectomy. Although all our patients have had an uneventful recovery, we find the high incidence of

ventricular arrhythmias quite disturbing. It has recently been found that the incidence is much lower in intubated children (Sigurdsson and Lindahl, 1983). This is one of the reasons why we nowadays prefer to intubate our patients for adenoidectomy.

#### ACKNOWLEDGEMENTS

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IV.

## INFLUENCE OF PREMEDICATION ON PLASMA ACTH AND CORTISOL CONCENTRATIONS IN CHILDREN DURING ADENOIDECTOMY

G. SIGURDSSON, S. LINDAHL AND N. NORDÉN

### SUMMARY

The endocrine response to stress, as reflected by the plasma concentrations of ACTH and cortisol, was investigated in 14 children receiving two different premedications during halothane anaesthesia for adenoidectomy. Seven children (group A) were premedicated with diazepam 5 mg rectally and atropine 0.3–0.4 mg sublingually and seven (group B) received a rectal combination of diazepam 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>. Before and after surgery plasma concentrations of ACTH and cortisol were lower in group B than in group A. In group A mean values for ACTH increased from 40.7 ng litre<sup>-1</sup> before adenoidectomy to 352.9 ng litre<sup>-1</sup> ( $P < 0.001$ ) after adenoidectomy. The corresponding increase in group B was from 12.1 ng litre<sup>-1</sup> to 82.1 ng litre<sup>-1</sup> ( $P < 0.01$ ). In group A mean cortisol concentrations increased from 235.7 nmol litre<sup>-1</sup> to 655.7 nmol litre<sup>-1</sup> after adenoidectomy ( $P < 0.001$ ) and in group B from 121.4 nmol litre<sup>-1</sup> to 427.9 nmol litre<sup>-1</sup> ( $P < 0.01$ ). End-tidal carbon dioxide tension was approximately the same in both groups. It was concluded that the combination of diazepam, morphine and hyoscine decreased the endocrine response to stress.

Although the plasma concentrations of ACTH and cortisol are increased during surgery (Sandberg, Eik-Nes and Samuels, 1954; Hume, Bell and Barker, 1962; Ichikawa et al., 1971) this response can be obtunded by high doses of morphine and fentanyl, and by extradural anaesthesia (George et al., 1974; Engqvist et al., 1977; Hall et al., 1978; Brandt et al., 1978). Since the influence of premedication on the endocrine response to preoperative anxiety and to surgical stimuli, as reflected by plasma concentrations of ACTH and cortisol, has not been reported previously, this study compared the plasma concentrations of ACTH and cortisol following the administration of two different premedications to children undergoing adenoidectomy.

### PATIENTS AND METHODS

Fourteen children scheduled for adenoidectomy were studied, none of whom had any evidence of acute infection, cardiac failure or pulmonary disease. All the children were fasted overnight and were randomly divided into two equal groups, A and B. In group A the mean age was 5 (range 3–7) yr with a mean body weight of  $20.4 \pm 3.2$  (SD) kg and in group B, mean age was 4 (range 3–6) yr with a

mean body weight of  $17.1 \pm 2.5$  (SD) kg. The children in group A were premedicated with diazepam 5 mg (Stesolid) rectally, that is about 0.25 mg kg<sup>-1</sup>, and atropine 0.3–0.4 mg sublingually 20–40 min before the induction of anaesthesia. Group B was premedicated with a rectal solution of diazepam (Apozepam) 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>, 30–40 min before the induction of anaesthesia.

Subsequently, whilst the child was still awake and in the presence of one of the parents, e.c.g. electrodes were applied. A photoelectric transducer (Siemens-Eléma, Stockholm) (Baselius and Nordström, 1971), for assessment of capillary perfusion, was attached to the distal part of the flexor side of the thumb and an arterial pressure cuff of appropriate size was placed around the left arm.

Both groups were anaesthetized by the same anaesthetist, who was not informed of the premedication used. Before induction of anaesthesia the anaesthetist evaluated the sedative effect of the premedication according to a modification of the method described by Barker and Nisbet (1973) (table I). During induction the anaesthetist also evaluated the antisialagogue effect as adequate (0) or inadequate (–). Inhalation anaesthesia with nitrous oxide in oxygen ( $FI_{O_2}$  0.5) and halothane (maximum concentration 2.5%) was used. An oral endotracheal tube was inserted in all of the children without the

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TABLE I. *Evaluation of premedication*

|                                           | Score |
|-------------------------------------------|-------|
| (I) Behaviour of the child                |       |
| Crying or struggling                      | 0     |
| Calm                                      | 1     |
| Sedated                                   | 2     |
| Drowsy                                    | 3     |
| Sleeping but arousable                    | 4     |
| (II) Reaction to induction of anaesthesia |       |
| Crying or struggling                      | 0     |
| Wincing or vocalizing                     | 1     |
| Moving the hands or head                  | 2     |
| None                                      | 3     |
| Estimation of sedation (I + II)           |       |
| 0-1.9 = poor                              |       |
| 2-3.9 = fair                              |       |
| 4-5.9 = good                              |       |
| 6-7.9 = excellent                         |       |

use of neuromuscular blocking drugs. Respiration was spontaneous. Rotameters for oxygen and nitrous oxide, and the Mark III halothane vaporizer, were calibrated. A Mapleson D circuit with fresh gas flows of three times the minute ventilation of the child was used to avoid rebreathing. During the induction of anaesthesia an infra-red carbon dioxide analyser (Siemens-Elema, Stockholm, 130) (Olsson et al., 1980) was incorporated in the anaesthetic circuit.

E.c.g., capillary perfusion (CP) and end-tidal carbon dioxide tension ( $PE'CO_2$ ) were recorded continuously (Siemens-Elema, EM81). Heart rate (HR) and breathing frequency were calculated from e.c.g. recordings and end-tidal carbon dioxide curves, respectively. Systolic and diastolic arterial pressures were measured intermittently and the mean arterial pressure (m.a.p.) calculated. The carbon dioxide analyser was calibrated using two test gases of known carbon dioxide concentration. Because of dispersion of the infra-red spectrum by nitrous oxide, all carbon dioxide values were corrected by a factor of 0.95 which referred to 50% nitrous oxide.

After the induction of anaesthesia a vein on the extensor side of the hand was cannulated to allow blood sampling. Samples for the measurement of ACTH and cortisol concentrations were collected in test tubes containing EDTA (10.5 mg/7 ml blood) and aprotinin (Trasylol, Bayer, Germany, 3000 KIE/7 ml blood) which had been pre-chilled on ice-water. The samples were kept at 0 °C until

centrifugation in a refrigerated centrifuge. The supernatants were then stored at -20 °C. The concentration of ACTH was determined by radioimmunoassay (ACTHK, Sorin Biomedica, Italy) using rabbit antiserum raised against porcine ACTH coupled to bovine albumin. Human ACTH was used as standard and  $^{125}I$ -ACTH as tracer. The coefficient of variation in duplicate determinations was 17% for values less than 50 ng litre<sup>-1</sup> and 10% for values greater than 50 ng litre<sup>-1</sup> (Hedner, Nordén and Valdemarsson, 1981). Cortisol concentration was determined using a solid phase radioimmunoassay (Gammacoat, Clinical Assays, Mass., U.S.A.) with rabbit anti-cortisol serum attached to the test tubes as binding protein and  $^{125}I$ -cortisol as tracer. The coefficient of variation was less than 7%. The cross reactivity was 88% for prednisolone and insignificant for other steroids tested.

Blood samples for analysis of venous oxygen ( $PvO_2$ ) and carbon dioxide ( $PvCO_2$ ) tension were taken in syringes and kept on ice until the analyses were performed 10 min later (IL 413, Instrumentation Laboratories, Italy).

#### Measurements

For the evaluation of relative changes in capillary perfusion the amplitude obtained during undisturbed anaesthesia and before intubation of the trachea ( $An$ , see below) was chosen as reference.

E.c.g., CP, MAP and  $PE'CO_2$  were measured at the following stages of anaesthesia and adenoidectomy: B = Before induction of anaesthesia; S = after induction of Sleep;  $An$  = during undisturbed Anaesthesia before intubation; Int = 1 min after Intubation; Ad = during Adenoidectomy; aAd = after Adenoidectomy; Ext = after Extubation; P = 15 min Post-op.

Blood samples were taken at stages  $An$  (sample 1), aAd (sample 2) and P (sample 3).

#### Statistics

Comparisons between the groups were carried out with paired Student's *t* test and the Chi-square test.

### RESULTS

#### Sedative effects

The evaluation of the sedative effects showed that the scores (table I) were greater in group B than in group A (table II). However, these differences were not significant.

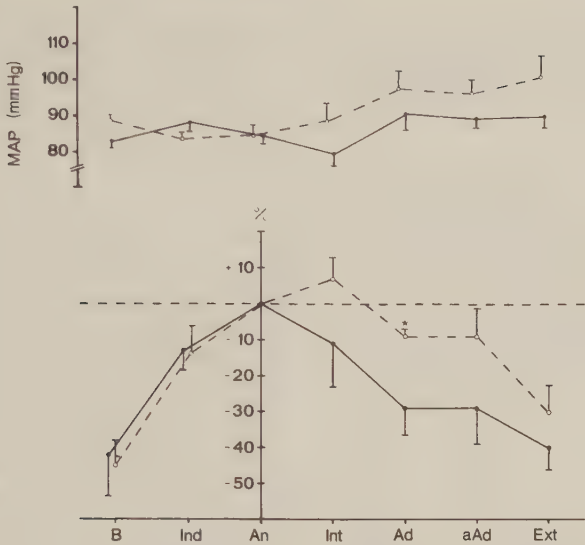


FIG. 1. Upper panel: Mean values  $\pm$  SEM for mean arterial pressure (MAP). Lower panel: Mean values  $\pm$  SEM for capillary perfusion during anaesthesia and adenoidectomy as related to the values at undisturbed anaesthesia (An). Group A ( $\circ$ --- $\circ$ ), group B ( $\bullet$ — $\bullet$ ).

TABLE II. Evaluation of sedation

|   |                       | Summary |   |   |   |   |   |   |
|---|-----------------------|---------|---|---|---|---|---|---|
| A | Sedation              | 3       | 4 | 4 | 3 | 3 | 3 | 4 |
|   | Antisialagogue effect | —       | 0 | 0 | 0 | 0 | — | — |
| B | Sedation              | 4       | 3 | 5 | 5 | 2 | 5 | 4 |
|   | Antisialagogue effect | 0       | 0 | 0 | 0 | 0 | 0 | — |

*Heart rate, mean arterial pressure, capillary perfusion and cardiac arrhythmias*

In both groups HR increased by about 30% during the procedure. MAP and CP were somewhat lower in group B after anaesthesia than in group A (fig. 1). At Ad capillary perfusion was significantly greater in group A than in group B ( $P < 0.05$ ). Four children in each group had supraventricular cardiac arrhythmia. In group A, three children also developed ventricular arrhythmia, while none was seen in group B.

*ACTH*

Plasma concentrations of ACTH at An and P were significantly less in group B than in group A ( $P < 0.01$  and  $P < 0.001$ , respectively, fig. 2). The

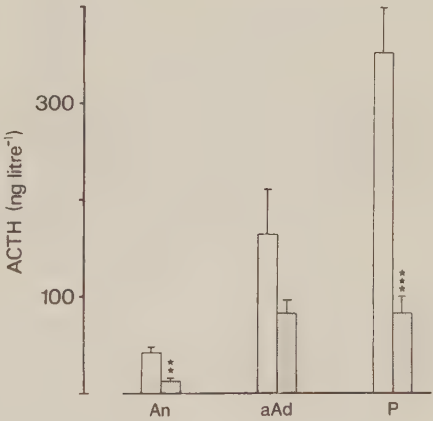


FIG. 2. Mean values  $\pm$  SEM for plasma concentrations of ACTH at An, aAd and P for group A (white columns) and for group B (stippled columns). \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

values (mean  $\pm$  SEM) in group A increased from  $40.7 \pm 6.5$  ng litre $^{-1}$  at An to  $352.9 \pm 46.5$  ng litre $^{-1}$  at P ( $P < 0.001$ ). The corresponding increase in group B was from  $12.1 \pm 2.0$  ng litre $^{-1}$  to  $82.1 \pm 17.3$  ng litre $^{-1}$  ( $P < 0.01$ ).

### Cortisol

Plasma cortisol concentrations were significantly lower in group B compared with group A ( $P < 0.01$ ,  $P < 0.001$  and  $P < 0.01$ , respectively, fig. 3). The values (mean  $\pm$  SEM) in group A increased from  $235.7 \pm 36.1$  nmol litre $^{-1}$  at An to  $655.7 \pm 18.4$  nmol litre $^{-1}$  at P ( $P < 0.001$ ). In group B the corresponding increase was from  $121.4 \pm 15.2$  nmol litre $^{-1}$  to  $427.9 \pm 63.3$  nmol litre $^{-1}$  ( $P < 0.01$ ).

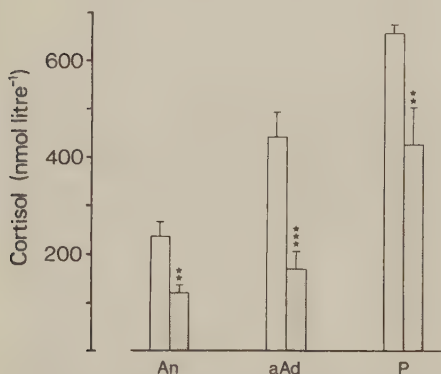


FIG. 3. Mean values  $\pm$  SEM for plasma concentrations of cortisol at An, aAd and P for group A (white columns) and for group B (stippled columns). \*\* $P < 0.01$  and \*\*\* $P < 0.001$ .

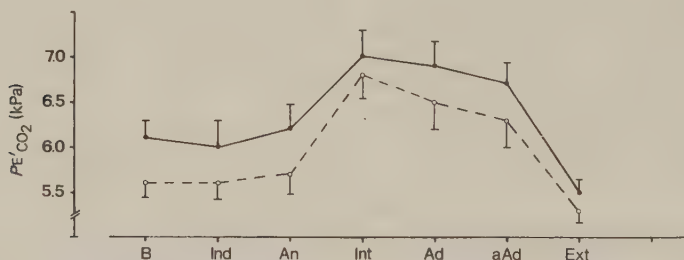


FIG. 4. End-tidal carbon dioxide tensions ( $PE'CO_2$ , kPa) for group A (dotted line) and for group B (continuous line). Mean values  $\pm$  SEM.

### Gas exchange

There was a statistically significant increase in respiratory rate and  $PE'CO_2$  in both groups during anaesthesia and surgery, but there were no significant differences between the groups (fig. 4). Venous oxygen and carbon dioxide tensions were normal in both groups.

### DISCUSSION

To avoid the diurnal variations in ACTH and plasma cortisol concentrations (Nilsson, Arner and Hedner, 1963) all children were investigated between 8.30 and 10.30 am. In both groups premedication was administered between 20 and 40 min before the induction of anaesthesia. Standardized methods for anaesthesia and surgery were used. Mean age, body weight and preoperative fasting were comparable in the two groups.

The anaesthetist judged the sedative and antistress effect of the premedication used in group B to be somewhat better than in group A. The material is, however, too small for any conclusions to be drawn on sedative effects, but the results confirm earlier reports that the combination of diazepam, morphine and hyoscine is advantageous (Lindahl, Olsson and Thomson, 1981).

Surgical procedures result in an increase in plasma cortisol concentration (Sandberg, Eik-Nes and Samuels, 1954; Cooper and Nelson, 1962; Hume, Bell and Barter, 1962; Nilsson, Arner and Hedner, 1963) and the secretion of ACTH increases rapidly after the skin incision (Ichikawa et al., 1971), which is relevant in this study since the time between the first and second blood samples was only 5–10 min. In other words, ACTH and cortisol are suitable indices of the endocrine stress response during short



procedures like adenoidectomy. The method used for the analysis of ACTH is known to give spurious values outside the normal range in about 2% of measurements (Hedner, Nordén and Valdemarsson, 1981). Obviously increased values were not observed in the unstressed state in the present clinical material.

It is also known that ACTH often reaches plasma concentrations above the concentration required for maximal corticosteroid output from the adrenals (Ganong, Alpert and Lee, 1974). Simultaneous analyses of plasma concentrations of ACTH and cortisol revealed a discrepancy in relative changes of plasma concentrations between ACTH and cortisol. ACTH concentrations increased more than eight times the initial value in group A, while the corresponding cortisol plasma concentrations increased less than three-fold. This supports the findings of Ganong, Alpert and Lee (1974), and demonstrates the inability of the adrenals to respond to the full ACTH stimulus.

Plasma concentrations of ACTH and cortisol were both significantly smaller in group B compared with group A, a result which, to some extent, might be explained by a decrease in anxiety. It was shown that, compared with the initial values of ACTH and cortisol during undisturbed anaesthesia, the increase after surgery was greater in group A than in group B. This cannot be explained by a decrease in anxiety alone. The suppressed ACTH and cortisol responses found in group B (premedicated with diazepam, morphine and hyoscine) might be a result of the morphine. However, the doses of morphine were small compared with those ( $1-4 \text{ mg kg}^{-1}$ ), described previously to block the ACTH and cortisol responses to surgery and stress (Reier, George and Kilman, 1973; George et al., 1974; Brandt et al., 1978).

The effect of diazepam in decreasing anxiety before operation is well documented (Tornetta, 1965; Dobkin et al., 1970) and Oyama and colleagues (1969) found that diazepam  $0.2 \text{ mg kg}^{-1}$  decreased the plasma free cortisol concentration. However, the sedative effect of diazepam is dose-dependent, even though there are great individual variations in the response to the drug (Brown and Dundee, 1968). Therefore, the differences in hormonal stress response between the two groups might to a large extent be explained by the larger dose of diazepam used in group B.

In addition, it has been shown that diazepam increases the effects of pethidine, morphine and

hyoscine when used in various combinations (Dundee et al., 1970). We feel that these additive effects were most probably the explanation of the clearcut differences in endocrine stress response demonstrated in this study.

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## DER EINFLUSS DER PRÄMEDIKATION AUF DIE PLASMA-ACTH- UND -CORTISOLKONZENTRATIONEN BEI KINDERN WÄHREND ADENEKТОMIE

### ZUSAMMENFASSUNG

Die endokrinische Antwort auf Stress, wie sie in den Plasma-Cortisol- und -ACTH-Konzentrationen zum Ausdruck kommt, wurde bei 14 Kindern, die zwei verschiedene Arten von Prämedikation erhalten hatten, während einer Halothannarkose bei der Adenektomie untersucht. Sieben Kinder (Gruppe A) wurden mit Diazepam 5 mg rektal und 0,3–0,4 mg Atropin sublingual prämediziert, und sieben (Gruppe B) mit einer rektalen Kombination von Diazepam 0,5 mg kg<sup>-1</sup>, Morphinum 0,15 mg kg<sup>-1</sup> und Skopolamin 0,01 mg kg<sup>-1</sup>. Vor und nach der Operation waren die Plasmakonzentrationen von ACTH und Cortisol niedriger in der Gruppe B als in Gruppe A. In Gruppe A stiegen die Durchschnittswerte von ACTH von 40,7 ng litre<sup>-1</sup> vor der Operation auf 352,9 ng litre<sup>-1</sup> ( $P < 0,001$ ) nach der Adenektomie an. Der entsprechende Anstieg in Gruppe B ging von 12,1 ng litre<sup>-1</sup> auf 82,1 ng litre<sup>-1</sup> ( $P < 0,01$ ). In Gruppe A stiegen die mittleren Cortisolkonzentrationen von 235,7 nmol litre<sup>-1</sup> auf 655,7 nmol litre<sup>-1</sup> nach der Adenektomie ( $P < 0,001$ ) und in Gruppe B von 121,4 nmol litre<sup>-1</sup> auf 427,9 nmol litre<sup>-1</sup> ( $P < 0,01$ ). Die endexpiratorische CO<sub>2</sub>-Spannung war etwa gleich in beiden Gruppen. Daraus wurde geschlossen, daß die Kombination von Diazepam, Morphinum und Skopolamin die endokrine Stressreaktion herabsetzt.

## INFLUENCE DE LA PREMEDICATION SUR DES CONCENTRATIONS PLASMATIQUES d'ACTH ET DE CORTISOL CHEZ DES ENFANTS SUBISSANT UNE ADENOIDECTOMIE

### RESUME

La réponse endocrinienne au stress, représentée par les concentrations plasmatiques d'ACTH et de cortisol, a été étudiée au cours d'une anesthésie à l'halothane pour adénoïdectomie chez 14 enfants ayant reçu l'une ou l'autre de deux prémédications différentes. Sept enfants (groupe A) étaient prémédiqués par 5 mg de diazépam par voie rectale et 0,3 à 0,4 mg d'atropine par voie sublinguale et sept enfants (groupe B) recevaient, par voie rectale, une association de diazépam 0,5 mg kg<sup>-1</sup>, morphine 0,15 mg kg<sup>-1</sup> et hyoscine 0,01 mg kg<sup>-1</sup>. Avant et après la chirurgie, les concentrations plasmatiques d'ACTH et de cortisol étaient plus basses dans le groupe B que dans le groupe A. Dans le groupe A, les valeurs moyennes de l'ACTH augmentaient de 40,7 ng litre<sup>-1</sup> avant l'adénoïdectomie à 352,9 ng litre<sup>-1</sup> ( $P < 0,001$ ) après l'adénoïdectomie. L'augmentation correspondante dans le groupe B était de 12,1 ng litre<sup>-1</sup> à 82,1 ng litre<sup>-1</sup> ( $P < 0,01$ ). Dans le groupe A, les concentrations moyennes de cortisol augmentaient de 235,7 nmol nmol litre<sup>-1</sup> à 655,7 nmol litre<sup>-1</sup> après adénoïdectomie ( $P < 0,001$ ) et dans le groupe B de 121,4 nmol litre<sup>-1</sup> à 427,9 nmol litre<sup>-1</sup> ( $P < 0,01$ ). La CO<sub>2</sub> de fin d'expiration était à peu près la même dans les deux groupes. Nous en concluons que l'association de diazépam, morphine et hyoscine diminue la réponse endocrinienne au stress.

## INFLUENCIA DE LA PREMEDICACIÓN SOBRE LAS CONCENTRACIONES DE ACTH Y DE CORTISOL EN EL PLASMA EN NIÑOS SOMETIDOS A ADENOIDECTOMIA

### SUMARIO

En 14 niños que recibían dos premedicaciones distintas durante la anestesia por halotano a someterse a una adenoidectomía, se averiguó la respuesta endocrina a la tensión, tal como reflejada por las concentraciones de ACTH y de cortisol en el plasma. A siete niños (grupo A), se les administró como premedicación 5 mg de diazepam rectalmente y 0,3–0,4 mg de atropina bajo la lengua y a los siete niños del grupo B, una combinación rectal de 0,5 mg kg<sup>-1</sup> de diazepam, 0,15 mg kg<sup>-1</sup> de morfina y 0,01 mg kg<sup>-1</sup> de hiascina. Antes y después de la operación, las concentraciones de ACTH y de cortisol en el plasma eran más bajas en el grupo B que en el grupo A. En el grupo A, los valores medios del ACTH aumentaron desde 40,7 ng litre<sup>-1</sup> antes de la adenoidectomía hasta 352,9 ng litre<sup>-1</sup> ( $P < 0,001$ ) después de la adenoidectomía. El aumento correspondiente en el grupo B fue de 12,1 ng litre<sup>-1</sup> a 82,1 ng litre<sup>-1</sup> ( $P < 0,01$ ). En el grupo A, las concentraciones medias de cortisol aumentaron desde 235,8 nmol litre<sup>-1</sup> hasta 655,7 nmol litre<sup>-1</sup> después de la adenoidectomía ( $P < 0,001$ ) y en el grupo B de 121,4 nmol litre<sup>-1</sup> a 427,9 nmol litre<sup>-1</sup> ( $P < 0,01$ ). La tensión respiratoria terminal de anhídrido carbónico era más o menos igual en ambos grupos. Se concluyó que la combinación de diazepam, morfina y hiascina hace disminuir la respuesta endocrina a la tensión.



CATECHOLAMINE AND ENDOCRINE RESPONSE IN CHILDREN  
DURING HALOTHANE AND ENFLURANE ANAESTHESIA FOR  
ADENOIDECTOMY

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In 28 children undergoing adenoidectomy plasma concentrations of catecholamines, ACTH and cortisol were measured. Fourteen children were anaesthetized with halothane (7 non-intubated, 7 intubated) and fourteen with enflurane (7 non-intubated, 7 intubated). During undisturbed anaesthesia plasma catecholamines were significantly higher with halothane, than with enflurane ( $p < 0.05$ ). Immediately after surgery catecholamines were increased up to 300 percent in the halothane groups. In the enflurane groups, however, the catecholamine concentrations remained unchanged. This difference between the two agents, after surgery, was statistically significant ( $p < 0.01$  for intubated and  $p < 0.001$  for non-intubated children). Fifteen minutes postoperatively no difference was found in plasma concentrations between the groups. In all four groups plasma concentrations of ACTH and cortisol increased similarly during the procedure.

It was concluded that plasma catecholamines were higher during halothane than during enflurane anaesthesia in children undergoing adenoidectomy. This difference may be caused by a stimulative effect of halothane on the endogenous catecholamine release. This increased sympathetic response during halothane anaesthesia was correlated to the incidence of ventricular arrhythmias previously found with this agent during adenoidectomy.

It has previously been shown that ventricular arrhythmias are less common with enflurane than with halothane anaesthesia (1,

2,3). The stability of cardiac rhythm during enflurane anaesthesia has also been demonstrated when sympathomimetic drugs are given (4,5,6). It has been suggested that this might be due to a decreased sensitivity of the myocardium to catecholamines when enflurane is used (7).

In an earlier investigation on children undergoing adenoidectomy it was observed that during surgery the heart rate increased significantly with halothane, but remained virtually unchanged with enflurane anaesthesia (3). Since this may indicate a difference between the agents in sympathetic stimulation, the aim of the present study was to elucidate catecholamine and endocrine response to adenoidectomy during halothane and enflurane anaesthesia in non-intubated and in intubated children.

## PATIENTS AND METHODS

Twenty-eight children undergoing adenoidectomy were studied. The children were randomly divided into four equal groups. Two groups were not intubated, one received halothane (group HN; age  $6.0 \pm 0.8$  yr) and the other enflurane (group EN; age  $5.6 \pm 1.1$  yr). Two groups were intubated receiving either halothane (group HI; age  $5.0 \pm 0.5$  yr) or enflurane (group EI; age  $5.4 \pm 1.1$  yr). All children were day-stay cases and belonged to ASA class I.

The children were premedicated with diazepam 5 mg (Stesolid<sup>R</sup>) rectally (approximately  $0.25 \text{ mg kg}^{-1}$ ) and atropine 0.3–0.4 mg sublingually 20–40 min before the induction of anaesthesia. With the child still awake and in the presence of one of its parents, E.C.G. electrodes were applied and an arterial pressure cuff was placed around the arm. A calibrated infra-red carbon dioxide analyzer (Siemens-Elerna, Stockholm, 130) (8) was incorporated in the anaesthetic circuit. Anaesthesia was induced with  $\text{O}_2/\text{N}_2\text{O}$  ( $\text{FiO}_2$  0.25) administered for one minute before halothane or enflurane was added and the  $\text{O}_2/\text{N}_2\text{O}$  ratio was adjusted to 1:1 ( $\text{FiO}_2$  0.5). The concentrations of halothane and enflurane were increased at intervals of 4–6 breaths, by steps of 0.5% and 1% respectively to a maximum of 2.5% for halothane and 5%

for enflurane. When the children in groups HN and EN were judged clinically to be adequately anaesthetized a mouth gag was inserted and the adenoidectomy was performed without endotracheal intubation or further supply of anaesthetics. The children in group HI and EI were intubated prior to surgery without the use of muscle relaxants and were anaesthetized throughout the procedure. All children were breathing spontaneously through a Mapleson D circuit. A fresh gas flow of 3 times the estimated minute ventilation was used to minimize rebreathing.

#### Biochemical methods

After the induction of anaesthesia a peripheral vein was cannulated for the sampling of blood. Samples for the analysis of ACTH and cortisol were collected in test tubes containing EDTA (10.5 mg/7 ml blood) and aprotinin (Trasylol<sup>R</sup>, Bayer, West Germany, 3000 KIE/7 ml blood) which had been prechilled in ice-water. The samples were kept at 0°C until centrifugation in a refrigerated centrifuge. The resulting plasma was then stored at -20°C. ACTH was determined by radioimmunoassay (ACTHK, Sorin Biomedica, Italy) using rabbit antiserum raised against porcine ACTH coupled to bovine serum albumin. Human ACTH was used as standard and <sup>125</sup>I-ACTH as tracer (9). Cortisol was determined using a solid phase radioimmunoassay (Gammacoat, Clinical Assays, Mass., USA) with rabbit anti-cortisol serum attached to the test tubes as binding protein and <sup>125</sup>I-Cortisol as tracer. Samples for measuring the total catecholamine concentration were drawn in tubes with 20 µl of anticoagulant and antioxidant (EGTA 90 mg/ml, glutathione 60 mg/ml and pH 6.0-7.4) per ml of blood. A modification of the radioenzymatic method of Passon and Peuler (10) (Upjohn Diagnostics, USA) based on rat liver catechol-O-methyltransferase and S-adenosyl-L-methionine-(<sup>3</sup>H-methyl) was used. After periodate oxidation the resulting <sup>3</sup>H-vanillin was extracted and measured by liquid scintillation. Between-runs coefficient of variation for the assay is 4.7-6.5% depending on concentration. Normal values for adults are 0.8-2.4 nmol litre<sup>-1</sup>.

## Measurements

E.C.G. and end-tidal carbon dioxide tensions ( $P_{ET}CO_2$ ) were recorded continuously (Siemens-Elema, EM81). Heart rate (HR) and breathing frequency (bpm, f) were calculated from E.C.G. recordings and end-tidal carbon dioxide curves, respectively. Systolic and diastolic arterial pressures were measured once a minute by auscultation and the mean arterial pressure (MAP) calculated. Blood samples were taken:

- a) during undisturbed anaesthesia (3.5-4.5 min after start of induction)
- b) just after adenoidectomy
- c) 15 min postoperatively

## Statistical methods

Between-group comparisons were carried out with two-sided Student's t-test. Data are given as mean values  $\pm$  s.e. mean.

## RESULTS

Age, body weight (Table 1) and sedative effects of premedication were comparable in all groups. Induction time, duration of surgery and time for "partial recovery" are shown in Table 2. One child in group HI and five children in group EI reacted to intubation by closing of vocal cords or by coughing. Three children in the non-intubated enflurane group (EN) reacted to the mouth gag during surgery by swallowing or by involuntary movements of extremities. These reactions were not seen in the non-intubated halothane group (HN).

Table 1

Patient data, n = 7 in each group (mean values  $\pm$  s.e. mean)

|        | Group HN       | Group EN       | Group HI       | Group EI       |
|--------|----------------|----------------|----------------|----------------|
| Age    | 6.0 $\pm$ 0.8  | 5.6 $\pm$ 1.1  | 5.0 $\pm$ 0.5  | 5.4 $\pm$ 1.1  |
| Weight | 22.4 $\pm$ 1.4 | 22.3 $\pm$ 2.0 | 20.4 $\pm$ 1.2 | 20.1 $\pm$ 2.1 |

Table 2

Mean values ( $\pm$  s.e. mean) of induction time, time for surgery and time for "partial recovery" (when the child was extubated, breathing normally, swallowing and reacting in a lively way to painful stimuli, but still not awake) in seconds (s) for the different groups.

|                       | Group HN      | Group EN     | Group HI     | Group EI     |
|-----------------------|---------------|--------------|--------------|--------------|
| Induction time, s     | 390 $\pm$ 39  | 469 $\pm$ 22 | 435 $\pm$ 38 | 491 $\pm$ 21 |
| Time for surgery, s   | 184 $\pm$ 12* | 141 $\pm$ 17 | 191 $\pm$ 23 | 236 $\pm$ 42 |
| "Partial recovery", s | 141 $\pm$ 13  | 166 $\pm$ 10 | 273 $\pm$ 25 | 329 $\pm$ 18 |

\* =  $p < 0.05$  for the difference between groups HN and EN

During undisturbed anaesthesia (sample a) plasma catecholamines were significantly higher in the two halothane groups (HN and HI) as compared with in the groups anaesthetized with enflurane (EN and EI,  $p < 0.05$ , Fig. 1a and 1b). At this stage of anaesthesia no differences in plasma concentrations of ACTH and cortisol were found between the groups (Fig. 2a and 2b).

Immediately after surgery (sample b) mean values of plasma catecholamines increased markedly in the halothane groups (Fig. 1a and 1b). In children anaesthetized with enflurane mean values of plasma catecholamines were, however, unchanged. This difference was statistically significant (Fig. 1a and 1b,  $p < 0.001$  for groups HN and EN and  $p < 0.01$  for groups HI and EI). Corresponding mean values for plasma concentrations of ACTH and cortisol were comparable in all four groups (n.s. Fig. 2a and 2b).

Fifteen minutes postoperatively (sample c) the mean values of plasma catecholamines in the two halothane groups were somewhat lower than just after surgery, but increased in the enflurane groups (Fig. 1a and 1b). At this time plasma concentrations of ACTH and cortisol were also increased in all four groups compared with the plasma concentrations just after surgery. Between-



group comparisons revealed no statistical significant difference in ACTH and cortisol concentrations at this stage (Fig. 2a and 2b).

There were no statistically significant differences in heart rate or mean arterial blood pressure between the halothane and enflurane groups at the different stages investigated. Two children in group HN and three in group HI developed ventricular arrhythmias. In the enflurane groups no ventricular arrhythmias were observed.

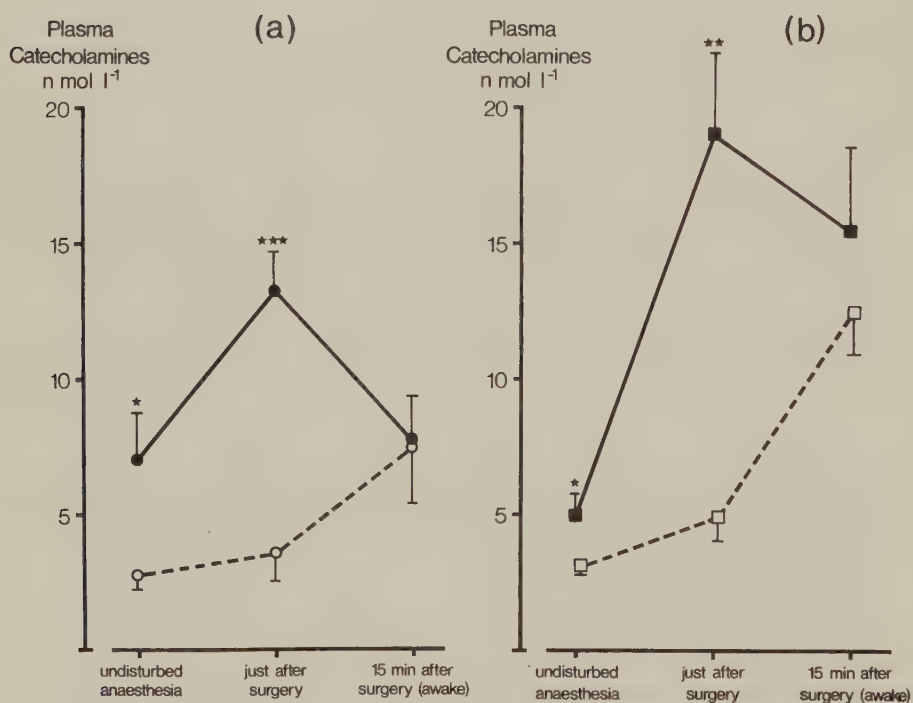


Fig. 1

Mean values  $\pm$  s.e. mean for plasma concentrations of catecholamines at the stages investigated

- a) in non-intubated children during halothane (filled circles, solid line) and enflurane anaesthesia (open circles, dotted line).
- b) in intubated children during halothane (filled squares, solid line) and enflurane anaesthesia (open squares, dotted line).

The mean  $P_{ET}CO_2$  increased in all groups during the procedure. The intubated groups had slightly higher mean values of  $P_{ET}CO_2$  than the non-intubated groups. The highest mean  $P_{ET}CO_2$  ( $\pm$  s.e. mean) were found after the intubation (in group HI  $6.8 \pm 0.3$  kPa and in group EI  $8.0 \pm 0.2$  kPa;  $p < 0.01$ ).

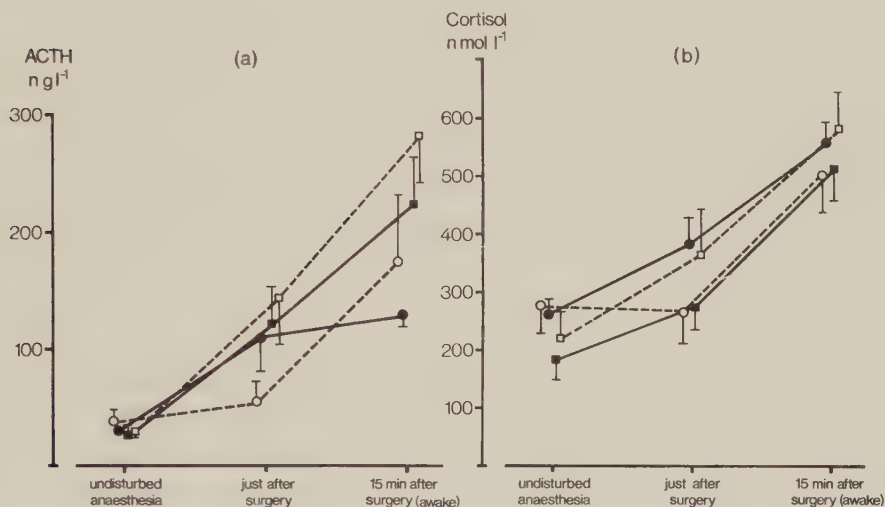


Fig. 2

Mean values  $\pm$  s.e. mean for plasma concentrations of ACTH (a) and cortisol (b) at the stages investigated (filled circles, solid line = halothane anaesthesia, non-intubation; filled squares, solid line = halothane anaesthesia, intubation; open circles, dotted line = enflurane anaesthesia, non-intubation; open squares, dotted line = enflurane anaesthesia, intubation).

## DISCUSSION

This study compared reactions to anaesthesia and surgery with two inhalational anaesthetics. The patients investigated were of comparable age and body weight and received identical pre-medication. All children were anaesthetized by the same

anaesthetist who was familiar with both anaesthetics used. The patients were also subjected to the same operative procedure. The anaesthetic technique was standardized as far as possible and comparable MAC values for the two agents from calibrated vaporizers were used. Ideally, static conditions with equilibrated inspired and expired gas concentrations indicated by end-tidal concentrations would also have been desired. However, to reach equilibrated gas conditions 20 to 30 min of anaesthesia is required, a duration which was not applicable in this investigation of a surgical procedure which normally only takes a few minutes. Furthermore, Eger and Bahlman (11) have shown that the estimation of anaesthetic level from end-tidal gas concentrations can be unreliable when the difference between inspired and expired gas concentrations is more than 0.5 percent, as was needed in the present series.

During undisturbed anaesthesia plasma catecholamines were significantly higher in the halothane than in the enflurane groups (Fig. 1a and 1b). Although, the action of halothane and enflurane on the sympathetic and endocrine function is not clearly defined in humans, Joyce and co-workers (12) recently showed increased noradrenaline release during inhalational induction of anaesthesia with halothane in adult volunteers. However, if the second stage of anaesthesia was circumvented by an intravenous injection of thiopentone before the addition of halothane the noradrenaline release was prevented (13). Joyce and co-workers (12) also found increased noradrenaline concentrations in cat spleen effluent, when the spleen was perfused with halothane. Furthermore, Sumikawa and co-workers (14) found that halothane caused a decreased uptake and an increased release of adrenaline from isolated bovine adrenal medullary chromaffin granules. On the other hand, *in vivo* (15) as well as *in vitro* (16) studies of enflurane have shown decreased catecholamine secretion from the adrenal medulla, which has been suggested to be due to a direct effect on the chromaffin cells (16). These clinical and experimental investigations may indicate that the difference in plasma catecholamines between halothane and enflurane during undisturbed anaesthesia found in this study may be caused by a specific effect of halothane on catecholamine release. The fact

that no difference was noted between the groups in ACTH and cortisol concentrations also indicates that the anaesthetics mainly influenced the catecholamine release directly rather than through effects on the central nervous system.

Plasma catecholamine concentrations were further increased just after surgery (sample b) in the halothane groups, while these remained unchanged during enflurane anaesthesia. This difference further emphasized the discrepancy in catecholamine release between enflurane and halothane discussed above. There was no difference in catecholamine response between non-intubated and intubated children anaesthetized with the same anaesthetic agent, neither between group HN and HI nor between group EN and EI (Fig. 1a and 1b). This in spite of the fact that no anaesthesia was given for 2 to 3 min during surgery (prior to sample b) in the non-intubated children (group HN and EN) while those who were intubated received anaesthesia during the whole procedure (group HI and EI). Thus, the catecholamine response to adenoidectomy in children seemed to be more dependent upon the choice of anaesthetic agent than the anaesthetic technique or the depth of anaesthesia.

That the catecholamine concentrations increased significantly in the enflurane groups and decreased in the halothane groups 15 min postoperatively, when the children were awake and crying, further supports the suggestion that enflurane reduced and halothane augmented catecholamine response during anaesthesia and surgery in these children (Fig. 1a and 1b).

Serious ventricular arrhythmias occur more frequently during halothane than during enflurane anaesthesia for adenoidectomy (3,17). They are most often seen during or just after surgery (3), which was correlated to the increased plasma catecholamine concentrations demonstrated in this investigation (Fig. 3). Previously it was suggested that this difference in incidence of ventricular arrhythmias was due to a decreased sensitivity of the myocardium to catecholamines with enflurane compared with halothane anaesthesia (7). The results of the present study, indicating suppressed catecholamine release with enflurane and

an increased release with halothane, give an additional explanation to the prominent difference in occurrence of ventricular arrhythmias between these two agents.

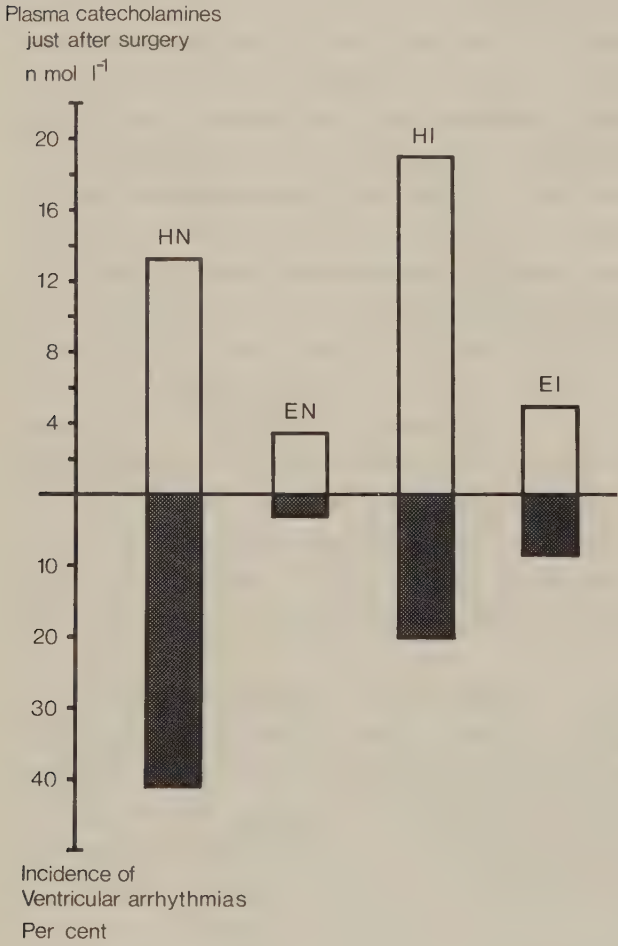


Fig. 3

The mean plasma catecholamine concentrations in the present study (unfilled columns) related to the incidence of ventricular arrhythmias (shaded columns) found in previous studies (3,17) using comparable methods.

HN = Halothane anaesthesia, non-intubation  
EN = Enflurane anaesthesia, non-intubation  
HI = Halothane anaesthesia, intubation  
EI = Enflurane anaesthesia, intubation



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## VI.

### INFLUENCE OF PREMEDICATION ON SYMPATHETIC - ENDOCRINE RESPONSE AND CARDIAC ARRHYTHMIAS DURING HALOTHANE ANAESTHESIA IN CHILDREN UNDERGOING ADENOIDECTOMY

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Cardiac arrhythmias were investigated in eighty children during halothane anaesthesia for adenoidectomy. Two different premedications were used. Forty children (group A) were premedicated with diazepam 5 mg rectally and atropine 0.3-0.4 mg sublingually and forty (group B) received a rectal solution including diazepam 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>. In seventeen of these children (9 in group A and 8 in group B) plasma concentrations of catecholamines, ACTH and corticosteroids were measured. In group A the mean plasma concentration of catecholamines increased more than 300 per cent during surgery, while it was virtually unchanged in group B. The difference between the two groups was statistically significant ( $p < 0.01$ ). Plasma concentrations of ACTH, cortisol and 17- $\alpha$ -hydroxyprogesterone were also higher in group A than in group B. The incidence of ventricular arrhythmias in group A was significantly higher (20%) than in group B (2.5%,  $p < 0.05$ ).

It was concluded that in these two comparable groups of patients the incidence of ventricular arrhythmias during halothane anaesthesia was nearly eliminated by the use of an improved premedication, due to a reduced sympathetic and endocrine response to surgery.

When halothane anaesthesia is used for oral surgery ventricular arrhythmias commonly occur, particularly during surgical stimulation (Tuohy, 1968; Ryder, 1970; Ryder and Townsend, 1974; Lindgren, 1981; Miller et al., 1970; Sigurdsson et al., 1983).

These arrhythmias can be prevented by beta-blockers or by blocking afferent impulses from the surgical field with local anaesthetics (Tolas and Allen, 1970; Rollason and Hall, 1973; Plowman, Thomas and Thurlow, 1974). This suggests that the common pathway for the development of these ventricular arrhythmias is a sympathetic stimulation of a myocardium sensitized for halothane (Katz and Bigger, 1970; Thurlow, 1972).

Influence of different anaesthetic methods on surgical stress has recently become the subject for many investigations, focused upon cortisol, growth hormone and catecholamine levels in plasma (Engquist et al., 1980; Kono et al., 1981; Glisson and Balasaraswathi, 1981; Roizen, Horrigan and Frazer, 1981). In a previous study on children undergoing adenoidectomy during halothane anaesthesia the influence of premedication on surgical stress as reflected by plasma concentrations of ACTH and cortisol was found to be decreased by a more efficient premedication (Sigurdsson, Lindahl and Nordén, 1982).

The aim of the present study was to investigate if this more efficient premedication (a rectal solution of diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$ ) also decreases catecholamine response and along with this to study the occurrence of ventricular arrhythmias in children undergoing adenoidectomy during halothane anaesthesia. Plasma concentrations of ACTH, cortisol and  $17\text{-}\alpha\text{-hydroxyprogesterone}$  were also measured.

## PATIENTS AND METHODS

Eighty children undergoing adenoidectomy were studied. No child had evidence of acute infection, or cardiopulmonary disease. The children were divided into two equal groups, A and B. In group A the mean age was 5.1 (range 2-12) yr and in group B 5.4 (range 1-12) yr. In seventeen children (9 in group A and 8 in group B), plasma catecholamines, ACTH, cortisol and  $17\text{-}\alpha\text{-hydroxyprogesterone}$  were measured. The mean age of the children in group A, in whom endogenic stress hormones were measured, was 4.9 (range 2-7) yr with a mean body weight of

19.8  $\pm$  3.4 (SD) kg. The corresponding mean age in group B was 4.6 (range 3-7) yr and a mean body weight of 17.9  $\pm$  3.1 (SD) kg.

The children in group A were premedicated with diazepam 5 mg (Stesolid<sup>R</sup>) rectally (about 0.25 mg kg<sup>-1</sup>) and atropine 0.3-0.4 mg sublingually. Group B was premedicated with a rectal solution of diazepam (Apozepam<sup>R</sup>) 0.5 mg kg<sup>-1</sup>, morphine 0.15 mg kg<sup>-1</sup> and hyoscine 0.01 mg kg<sup>-1</sup>. The premedication was ordered to be given 20-40 min before induction of anaesthesia.

E.c.g. electrodes were applied while the child was still awake and in the presence of one of its parents. An arterial pressure cuff of appropriate size was placed around the left arm. All children were anaesthetized by the same anaesthetist who was not informed of the premedication used. Before induction of anaesthesia the anaesthetist evaluated the sedative effect of the premedication according to a modification of the method described by Barker and Nisbet (1973) (Sigurdsson, Lindahl and Nordén, 1982).

Inhalation anaesthesia with nitrous oxide in oxygen (FiO<sub>2</sub> 0.5) and halothane (maximum concentration 2.5%) was used. An oral endotracheal tube was inserted in all children without the use of neuromuscular blocking drugs. Respiration was spontaneous. Rotameters for oxygen and nitrous oxide and a Mark III halothane vaporizer were calibrated. A Mapleson D circuit with fresh gas flows of three times the estimated minute ventilation of the child was used to avoid rebreathing. At the induction of anaesthesia an infra-red carbon dioxide analyzer (Siemens-Eléma, Stockholm, 130) (Olsson et al., 1980) was incorporated in the anaesthetic circuit. It was calibrated by the use of two test gases of known carbon dioxide concentrations within the measuring range. Because of dispersion of the infra-red spectrum by nitrous oxide, carbon dioxide values were corrected by a factor of 0.95. E.c.g. and end-tidal carbon dioxide tensions (P<sub>ET</sub>CO<sub>2</sub>) were recorded continuously (Siemens-Eléma, EM81). Heart rate (HR) and breathing frequency (bpm, f) were calculated from e.c.g. recordings and end-tidal carbon dioxide curves,



respectively. Systolic and diastolic arterial pressures were measured intermittently and the mean arterial pressure (MAP) calculated.

### Biochemical methods

After the induction of anaesthesia a peripheral vein was cannulated for the sampling of blood. Samples for the analysis of ACTH and cortisol were collected in test tubes containing EDTA (10.5 mg/7 ml blood) and aprotinin (Trasylo<sup>R</sup>, Bayer, West Germany, 3000 KIE/7 ml blood) which had been prechilled in ice-water. The samples were kept at 0°C until centrifugation in a refrigerated centrifuge. The resulting plasma was then stored at -20°C. ACTH was determined by radioimmunoassay (ACTHK, Sorin Biomedica, Italy) using rabbit antiserum raised against porcine ACTH coupled to bovine serum albumin. Human ACTH was used as standard and <sup>125</sup>I-ACTH as tracer (Sigurdsson, Lindahl and Nordén, 1982). Cortisol was determined using a solid phase radioimmunoassay (Gammacoat, Clinical Assays, Mass., USA) with rabbit anti-cortisol serum attached to the test tubes as binding protein and <sup>125</sup>I-cortisol as tracer. A radioimmunochemical method was also used for the assay of 17- $\alpha$ -hydroxyprogesterone (OHPK, Sorin Biomedica, Italy). The method was based on rabbit antibodies against the 3-conjugate to bovine serum albumin. The tracer was tritiated and dextran coated charcoal was used for separation. Samples for measuring the total catecholamine concentration were drawn in tubes with 20  $\mu$ l of anticoagulant and antioxidant (EGTA 90 mg/ml, glutathione 60 mg/ml and pH 6.0-7.4) per ml of blood. A modification of the radioenzymatic method of Passon and Peuler (1973) (Upjohn Diagnostics, USA) based on rat liver catechol-O-methyltransferase and S-adenosyl-L-methionine-(<sup>3</sup>H-methyl) was used. After periodate oxidation the resulting <sup>3</sup>H-vanillin was extracted and measured by liquid scintillation. Between-runs coefficient of variation for the assay is 4-10 percent depending on concentration. Normal values for adults are 0.8-2.4 nmol litre<sup>-1</sup>.

### Measurements

E.c.g., MAP, f and P<sub>ET</sub>CO<sub>2</sub> were measured at the following stages

- (1) before induction of anaesthesia
  - (2) after induction of sleep (approximately 2.5 min after start of induction)
  - (3) during undisturbed anaesthesia (3.5-4.5 min after start of induction)
  - (4) before intubation
  - (5) after intubation
  - (6) during adenoidectomy
  - (7) after adenoidectomy
  - (8) after extubation, when the child was breathing normally and was judged to control its airways adequately, swallowing and reacting in a lively way to painful stimuli, but still not awake, "partial recovery"
  - (9) 15 min postoperatively, when the child was awake.
- Blood samples were taken at stages 3, 7 and 9.

#### E.c.g. criteria

Sinus tachycardia (ST) was not classified as arrhythmia. A HR below  $60 \text{ min}^{-1}$  during 5 s or more was used as a criterion for sinus bradycardia (SB). Isolated ectopic beats were only reported when at least three were seen in the same child. Beats with bizarre QRS configurations were considered to be of ventricular origin (VES), unless there was positive evidence for a supra-ventricular origin. Three or more consecutive beats of ventricular origin were regarded as ventricular tachycardia (VT).

#### Statistical methods

The two-tailed F-test and Student's t-test were used to compare the variances and mean values in the two groups. When there was no significant difference in variance the pooled variance estimate was used in the t-test (Afifi and Azen, 1979). Otherwise the separate variance estimate of the level of significance was used. Stepwise linear discriminant analysis (Afifi and Azen, 1979) was used to find all variables that contribute significantly to the discrimination between the children in group A and B respectively. The Chi-square test was used to test significance in frequency of ventricular arrhythmias between the two groups.

## RESULTS

All children in group A and thirty-eight children in group B received their premedication between 25 and 50 min before induction of anaesthesia. One child in group B had its premedication 90 min and another 130 min before induction of anaesthesia. Mean sedative score ( $\pm$  SEM) for the premedication was significantly higher in group B ( $4.1 \pm 0.2$ , good) than in group A ( $3.0 \pm 0.2$ , fair,  $p < 0.001$ ). The mean induction time (i.e. the time until intubation) and the time for "partial recovery" (defined above) were comparable in the two groups (Table 1). A slight airway obstruction (stridorous breathing) was noted in three children of each group during the induction of anaesthesia (excitational stage). One child in group A had a slight airway obstruction just after extubation. These airway problems were, however, always shortlived and laryngospasm with cyanosis was not observed in any child. No airway problems were noted post-operatively. Reactions to intubation, such as coughing and closure of vocal cords, occurred in ten children in group A and in nine children in group B.

Table 1

Mean values ( $\pm$  SEM) for induction time, operation time and for "partial recovery" (see definition in the text) in seconds (s) for the two groups.

|                             | Group A          | Group B          |
|-----------------------------|------------------|------------------|
| Time for induction          | $388.0 \pm 15.5$ | $372.4 \pm 13.6$ |
| Time for adenoidectomy      | $249.6 \pm 12.8$ | $245.6 \pm 14.9$ |
| Time for "partial recovery" | $255.0 \pm 12.2$ | $262.4 \pm 10.5$ |

### Arrhythmias

Only those children who had a normal e.c.g. before anaesthesia were included in the study. The incidence and classification of arrhythmias are shown in Table 2. Arrhythmias were observed in twenty-six children in group A (65%) and in eighteen children in group B (45%). Junctional rhythm was the most common

arrhythmia in both groups. Eight children in group A (20%) and only one child in group B (2.5%) developed ventricular arrhythm-

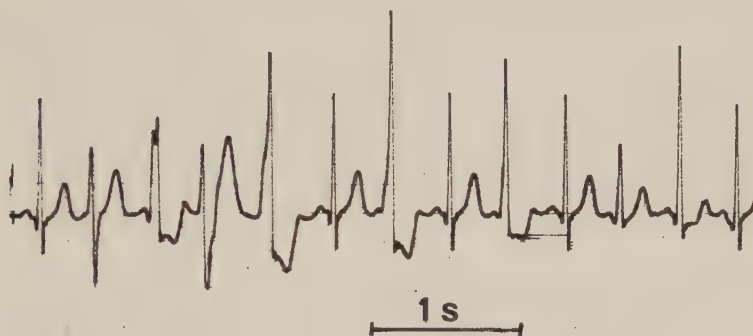


Fig. 1

E.c.g. (lead  $V_5$ ) in a 6 yr old boy. At the end of surgery he developed irregular ventricular arrhythmia at a rate of  $160 \text{ min}^{-1}$ . During the arrhythmia MAP was 115 mmHg, plasma catecholamines  $14.9 \text{ nmol litre}^{-1}$ ,  $P_{\text{ET}}\text{CO}_2$  6.7 kPa, venous  $\text{PCO}_2$  6.9 kPa and venous  $\text{PO}_2$  26.3 kPa.

Table 2

Classification of arrhythmias. Note that ventricular arrhythmias occurred in eight children in group A as compared with one in group B. VES = ventricular extra-systole (ventricul ectopic beat).

|                                   | n = 40<br>Group A | n = 40<br>Group B |
|-----------------------------------|-------------------|-------------------|
| Arrhythmias total                 | 26 (65%)          | 18 (45%)          |
| Supraventricular arrhythmias      | 19 (47.5%)        | 17 (42.5%)        |
| junctional rhythm                 | 16                | 16                |
| ectopic atrial rhythm             | 2                 | -                 |
| sinus bradycardia                 | 1                 | 1                 |
| Ventricular arrhythmias           | 8 (20%)*          | 1 (2.5%)          |
| unifocal VES or unifocal bigemini | 2                 | 1                 |
| multifocal VES                    | 2                 | -                 |
| ventricular tachycardia           | 4                 | -                 |

\* =  $p < 0.05$  for the difference between group A and B

thmia ( $p < 0.05$ ). Two of the children in group A had multifocal ventricular ectopic beats and four developed episodes of ventricular tachycardia with heart rate of  $140\text{--}200\text{ min}^{-1}$  (Fig. 1). The child in group B who developed ventricular arrhythmia had isolated unifocal ventricular ectopic beats for 40 s during surgery. Supraventricular arrhythmias were mostly seen during undisturbed anaesthesia, while ventricular arrhythmias occurred during or shortly after surgery.

The mean arterial pressure increased by almost 10 percent and the heart rate by 25–30 percent in both groups during surgery. No significant differences were found between the groups in mean arterial pressure, but pulse rates at stages 1,2,6,7 and 8 were among the variables which discriminated the groups.

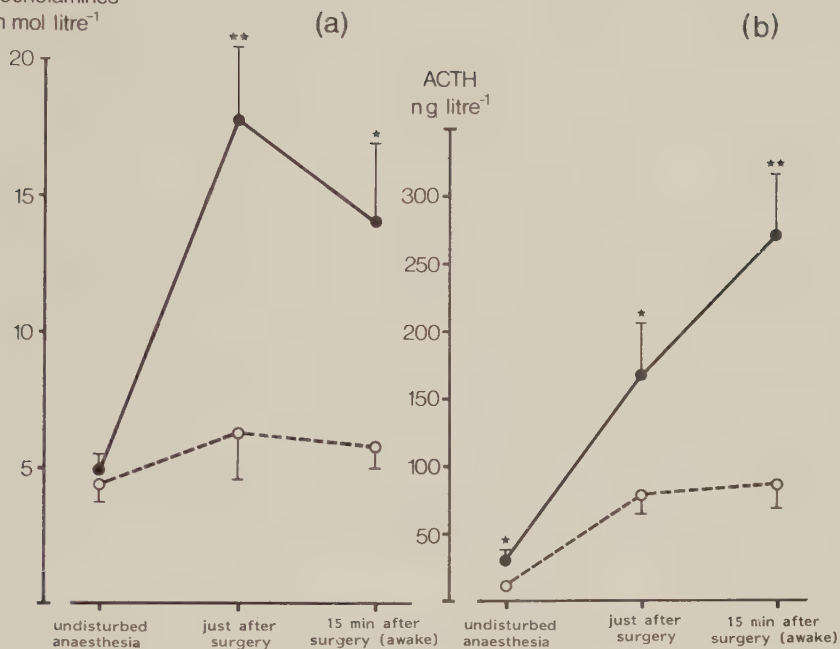
#### Total plasma catecholamines, ACTH, cortisol and 17- $\alpha$ -hydroxyprogesterone

During undisturbed anaesthesia there was no difference between the groups in catecholamine concentrations (Fig. 2a), but just after surgery and 15 min after surgery they were significantly higher in group A than in group B ( $p < 0.01$  and  $p < 0.05$ , respectively, Fig. 2a). In group A the mean ( $\pm$  SEM) concentration increased more than three times, from  $4.9 \pm 0.6\text{ nmol litre}^{-1}$  during undisturbed anaesthesia to  $17.9 \pm 2.7\text{ nmol litre}^{-1}$  just after surgery ( $p < 0.001$ ). In group B, there was no significant change in mean concentrations of catecholamines during the procedure. The mean plasma concentrations of ACTH, cortisol and 17- $\alpha$ -hydroxyprogesterone were higher at all measuring stages in group A than in group B (Fig. 2b,2c and 2d).

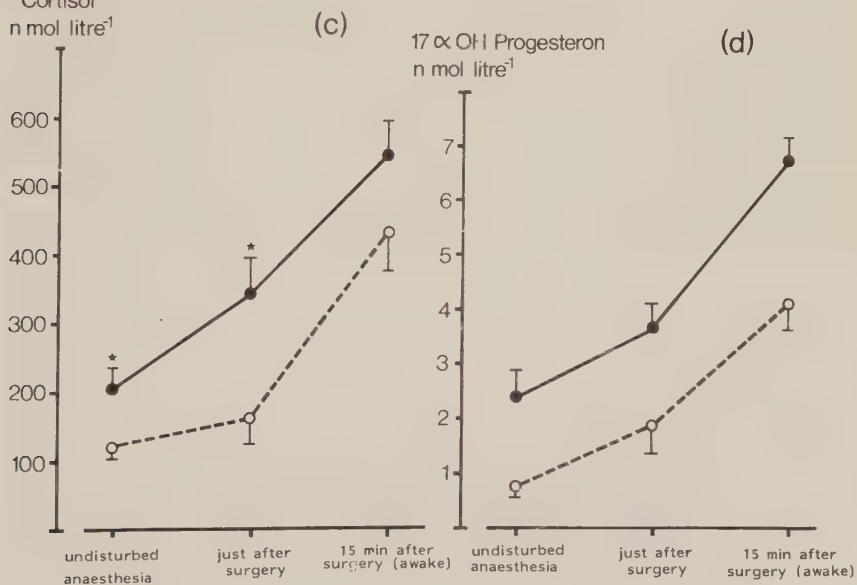
Fig. 2

Mean values  $\pm$  SEM for plasma concentrations of catecholamines (a), ACTH (b), cortisol (c) and 17- $\alpha$ -hydroxyprogesterone (d) at the various stages for group A ( $n = 9$ ; continuous line) and for group B ( $n = 8$ ; dotted line). \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$  for the difference between group A and B.

Plasma  
Catecholamines  
 $\text{n mol litre}^{-1}$



Cortisol  
 $\text{n mol litre}^{-1}$





## Gas exchange

In both groups respiratory rate and  $P_{ET}CO_2$  increased during undisturbed anaesthesia and surgery. The mean  $P_{ET}CO_2$  values were 0.1–0.4 kPa higher in group B than in group A at all stages, but this difference was not statistically significant. The highest  $P_{ET}CO_2$  values (mean  $\pm$  SEM) were found after intubation (stage 5) in both groups,  $6.5 \pm 0.1$  in group A and  $6.8 \pm 0.1$  in group B.

In the stepwise discriminant analysis the variables were entered into a discriminating function, provided that the variable gave a significant contribution at each step to the discrimination between group A and B. Thus ten of the twenty variables were found to contribute to this discrimination, including catecholamines and all hormones measured, as well as heart rate at various stages of the procedure. Using the final discrimination function it was possible to classify all patients in group A and B to the correct group, i.e. no miss-classification error occurred (Fig. 3).

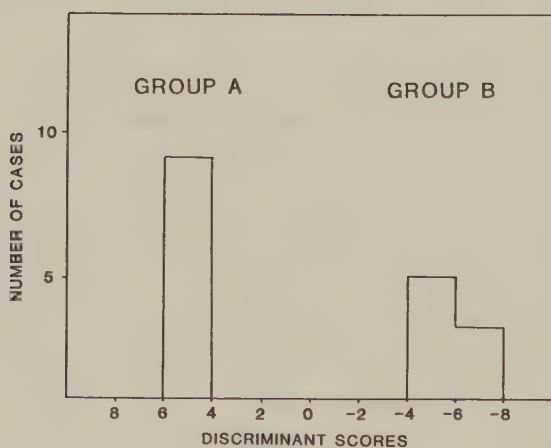


Fig. 3

The result of the stepwise discriminant analysis. A complete separation between group A and B was achieved with ten discrimination functions, including catecholamines, ACTH, cortisol, 17- $\alpha$ -hydroxyprogesterone, as well as heart rate at stages 1,2,6,7 and 8.

## DISCUSSION

A few decades ago an efficient premedication was considered to be of great clinical importance to reduce salivation and laryngeal reflexes as well as to come across the excitational stage smoothly. Since the development of newer and more effective inhalational anaesthetics it has been suggested that these premedication advantages are less important and it has even been debated if premedication should be used at all. There are, however, reports saying that preoperative anxiety in children might result in psychological disturbances (Eckenhoff, 1953) and even increased peroperative bleeding (Haq and Dundee, 1968).

Recently it was shown that a premedication with rectal combination of diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$  reduced the endocrine response to surgery, when compared with a less sedative premedication, consisting of rectally administered diazepam in a dose of approximately  $0.25 \text{ mg kg}^{-1}$  and sublingual atropine in a dose of  $0.015 \text{ mg kg}^{-1}$  (Sigurdsson, Lindahl and Nordén, 1982). In the present study the same two premedications were used in two comparable groups of children subjected to adenoidectomy. The premedications were given 25–50 min before induction of anaesthesia, an interval during which peak plasma concentrations of rectally administered diazepam and morphine are known to occur (Lindahl, Olsson and Thomson, 1981; Westerling et al., 1982). That the premedication with diazepam, morphine and hyoscine resulted in a higher mean sedative score, was probably due to the higher diazepam dose used, combined with the sedative properties of morphine and hyoscine (Conner et al., 1977).

The patients who received the more sedative premedication also had lower plasma concentrations of ACTH, cortisol and  $17\text{-}\alpha\text{-}$ hydroxyprogesterone during undisturbed anaesthesia. Unexpectedly, however, the catecholamine concentrations were equally high in the two groups at this stage of anaesthesia. This may have been due to an increased catecholamine release during the second stage of anaesthesia, unaffected by the premedication used, which has been shown in adults after an inhalational induction with halothane (Joyce et al., 1982). Joyce, Roizen and

Eger (1981) have shown that if the excitational stage is circumvented by intravenous induction with thiopentone, before halothane is added, catecholamine release can be prevented. On the basis of these findings it may be emphasized that the second stage of anaesthesia probably still is of clinical importance in spite of the development of modern inhalational anaesthetics.

Although the more sedative premedication did not prevent increase in plasma catecholamines during induction of anaesthesia, it effectively reduced the catecholamine and endocrine response during surgery. Since diazepam decreases plasma catecholamines during morphine anaesthesia (Hoar et al., 1981) and since the central sedative effects of diazepam are dose dependent (Brown and Dundee, 1968), and have been attributed to an inhibitory action on cerebral sympathetic neurotransmitter activity (Biswas and Carlsson, 1978; Bertilsson, 1978), it may be suggested that the higher dose of diazepam used in the more efficient premedication contributed to the decreased catecholamine response to surgery. Furthermore, the analgetic and sedative effects of morphine potentiated by hyoscine probably had an additive effect.

It is well established that adrenergic activation does occur during surgical stress in man and this is not caused by anaesthesia alone (Halter, Pflug and Porte, 1977). It is also known that endogenous catecholamines and sympathomimetic drugs produce cardiac arrhythmias by increasing automaticity and stimulating ectopic pacemaker activity (Leon and Abrams, 1971). Halothane anaesthesia potentiates these effects (Katz and Bigger, 1970). In this study the incidence of ventricular arrhythmias in group A was 20 percent occurring during or immediately after surgery, when plasma concentrations of catecholamines were increased by more than 300 percent. In group B, however, only one child developed ventricular arrhythmia. In this group plasma catecholamines remained unchanged during surgery (Fig. 2a). The child who developed ventricular arrhythmia in this group received its premedication 130 min before induction of anaesthesia. This arrhythmia may very well have occurred due to a lowered protective effect of the premedication since diazepam and

morphine were probably both in the redistribution phase (Lindahl, Olsson and Thomson, 1981; Westerling et al., 1982).

The advantages of this more sedative premedication, in reducing the occurrence of ventricular arrhythmias during these short surgical procedures, were not complicated by a too heavy postoperative sedation. No child had any postoperative airway problems. At our hospital this premedication has during the last two years been used in more than 500 children subjected to adenoidectomy, without any postoperative airway complications. Furthermore, Haq and Dundee (1968) have shown a correlation between preoperative anxiety and increased bleeding in children undergoing adeno-tonsillectomy, emphasizing the importance of an adequate premedication for these operations.

In conclusion, it would appear that for this duration of surgery and degree of surgical stimulation, premedication with a rectal solution of diazepam  $0.5 \text{ mg kg}^{-1}$ , morphine  $0.15 \text{ mg kg}^{-1}$  and hyoscine  $0.01 \text{ mg kg}^{-1}$  effectively reduced the incidence of ventricular arrhythmias during halothane anaesthesia. This was due to reduced sympathetic activity found immediately after surgery. We believe that the additive central nervous effects of these drugs on preoperative anxiety and on afferent impulses from the surgical field account for the clear cut differences in sympathetic and endocrine response demonstrated in this study.

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